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EVENT-RELATED POTENTIALS AS A MEASURE OF SPEECH CUE PROCESSING IN NEWBORNS WITH GENETIC RISK FOR DYSLEXIA

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ABSTRACT

Differences in auditory brain event-related potentials (ERPs) between school-aged children with dyslexia and controls indicate underlying auditory processing differences that may be linked to speech sound processing problems in this disorder (Leppänen and Lyytinen, 1997). To test whether such deviations are already found early in development, we investigated the ERPs to speech sounds in newborns with a genetic risk for dyslexia (n=26) and infants without such risk (n=23).

We measured ERPs to synthetic and natural CV-syllables (/ba/, /da/, /ga/; /paa/, /taa/, /kaa/) presented with equal probability during quiet sleep. The ERPs were analyzed by the principal component analyses (PCA). Factor scores (four factors accounting for 89.3 % of the total variance in the synthetic /ba/, /da/, and /ga/ stimulus set, and four factors for 88.7 % of the total variance in the natural /paa/, /taa/, /kaa/ stimulus set) were selected for further MANOVA/ANOVA for repeated measures analyses. There were significant (*p*s <. 05) group-related interactions for all the first three factors for the synthetic stimuli set. The most interesting effect was found for Factor 3 (at the latency of 375-715 ms, with the maximum factor score at 565 ms): in the control group the factor scores for /ga/ were more positive in the left hemisphere, while in the at-risk group similar pattern occurred in the right hemisphere. For Factor 1 (between 565-950 ms, with a maximum at 855 ms), factor scores for /da/ were more positive than those for /ba/ in the parietal channels in the control group, but in the at-risk group this pattern was reversed. For Factor 2 (between 135-555 ms, with a maximum at 285 ms), factor scores for the parietal responses were more negative in the left hemisphere in the control group, but on the contrary, in the at-risk group the factor scores were more negative in the right hemisphere. In the natural stimuli set (in Factor 3 between 345-695 ms, with a maximum at 505 ms), when compared to the control group, the at-risk groups' factor scores for /kaa/ in the parietal sites did not differ from the scores for the central channels. These results partially replicated the findings of Molfese et al. (1979a, 1985, 1991, 1997).

Discriminant function analysis was used to test how well group membership (at-risk versus control) could be determined by the factor scores that contributed to group interactions in the ERP measures. The composite scores differentiated the groups with an accuracy of 91.84 % ($p < .003$). These results indicate that the cortical electric activation generated by speech elements is already different in infants at-risk for dyslexia at this early stage of development.

Keywords: brain event related potentials, newborns, developmental dyslexia, auditory processing, consonant differentiation, principal component analysis

TIIVISTELMÄ

Erot auditiivisissa herätevasteissa (ERP, event related potentials) kouluikäisten dyslektikkojen ja kontrollilapsien välillä viittaavat dysleksian taustalla oleviin auditiivisen prosessoinnin ongelmiin (Leppänen and Lyytinen, 1997). Halusimme selvittää voidaanko kyseisiä prosessoinnin eroja löytää jo kehityksen varhaisista vaiheista, joten valitsimme tutkimuksen kohteeksi vastasyntyneet, joilla oli perinnöllinen riski dysleksiaan.

Tutkimme synteettisten ja luonnollisten konsonantti-vokaali -tavujen synnyttämien ERP-vasteiden eroja riski- (n=26) ja kontrolliryhmän (n=23) välillä (synteettiset ärsykkeet /ba/, /da/, /ga/; sekä luonnolliset ärsykkeet /paa/, /taa/, /kaa/, esitetty samalla todennäköisyydellä koehenkilöiden ollessa syvässä unessa). ERP-aineisto analysoitiin pääkomponenttianalyysillä (PCA, principal component analysis) joka tiivistää ERP-aineistossa tapahtuvan systemaattisen vaihtelun faktori-pistemääriksi. Nämä pistemäärät (neljä faktoria, jotka selittivät 89.3 % kokonais-vaihtelusta synteettisten ärsykkeiden välillä, ja neljä faktoria, jotka vastaavasti selittivät 88.7 % kokonaisvaihtelusta luonnollisten ärsykkeiden välillä) toimivat lähtökohtina toistettujen mittausten MANOVA/ANOVA jatkoanalyyseille. Tilastollisesti merkitseviä ($p < .05$) ryhmien välisiä eroja löydettiin kolmelta ensimmäiseltä faktorilta synteettisten ärsykkeiden tilanteessa. Mielenkiintoisin näistä löytyi kolmannelta faktorilta (375-715 ms, huippu 565 ms): kontrolliryhmän faktoripisteet /ga/:han olivat positiivisemmat vasemmassa aivopuoliskossa, kun taas vastaava efekti oli riskiryhmässä oikeassa aivopuoliskossa. Ensimmäisellä faktorilla (565-950 ms, huippu 855 ms) kontrolliryhmän parietaalikanavien faktoripisteet /da/:han olivat positiivisemmat /ba/:han verrattuna. Vastaavasti riskiryhmässä tilanne oli päinvastainen. Toisella faktorilla (135-555 ms, huippu 285) kontrolliryhmän parietaalikanavien faktoripisteet olivat negatiivisemmat vasemmassa aivopuoliskossa, kun taas riskiryhmässä suurin negatiivisuus löytyi oikeasta aivopuoliskosta. Luonnollisten ärsykkeiden tilanteessa (kolmas faktori, 345-695 ms, huippu 505 ms) riskiryhmän parietaalikanavien faktoripisteet /kaa/:han eivät eronneet sentraalikanavista yhtä selvästi kuin kontrolliryhmän vastaavat pistemäärät. Nämä tulokset ovat osittain yhdenmukaisia Molfesen ym. (1979a, 1985, 1991, 1997) tulosten kanssa.

Erotteluanalyysiin (discriminant function analysis) valittiin muuttujat, jotka vaikuttivat saatuihin ryhmäeroihin synteettisten ja luonnollisten ärsykkeiden tilanteissa. Muuttujat luokittelivat koehenkilöt riski- ja kontrolliryhmiin 91.84 % tarkkuudella ($p < .003$). Nämä tulokset osoittavat, että jo tässä varhaisessa kehityksen vaiheessa puheäänien synnyttämä aivojen aktivaatio on erilaista vauvoilla, joilla on perinnöllinen dysleksiariski.

Avainsanat: herätevasteet, vastasyntyneet, kehityksellinen dysleksia, auditiivinen prosessointi, konsonanttien erottelu, pääkomponenttianalyysi

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CONTENTS

1. INTRODUCTION

This study is part of the larger longitudinal JLD-project (Jyväskylä Longitudinal Study of Dyslexia). One of the goals of this project is to search precursors of dyslexia and to follow the development of language acquisition from birth to school age. The participants in this project belong to either of the two main groups: a sample of families in which a child (children) is born with genetic risk for dyslexia, or a matched sample of families where a child (children) does not have this risk. The criteria for inclusion in the genetic risk group are diagnosed dyslexia of one of the parents and reported dyslexia by some other close relative of that parent. A more comprehensive description of this follow-up project can be found in the articles of Lyytinen (1997), and Lyytinen, Leinonen, Nikula, Aro, and Leiwo (1995).

Reading is based on a complex set of skills and cognitive processes. In dyslexia, however, these skills are not acquired normally. The underlying causes of this failure are largely unknown. One of the possible causes of this reading problem is a deficit in phonological processing (Brady and Shankweiler, 1991; Catts, 1991). According to Wagner and Torgesen (1987), phonological processing can be conceptualized as encompassing at least three different components or skills: phonological awareness, phonological recoding in lexical access, and in short-term verbal memory. Of these three subskills phonological awareness appears to be the most deficient linguistic skill in disabled readers (Lyon, 1995). Performance on phonological awareness tasks has been one of the best predictors of early reading acquisition (Bradley and Bryant, 1978, 1983).

But is there a possibility that these problems in dyslexia, which are manifested in phonological processes could also be seen in lower level of functioning? And further, could these deficits be already recognized before the emergence of some developmentally higher cognitive ability such as language acquisition? It is reasonable to assume, as is suggested, for example, by Fitch, Miller, and Tallal (1997), that in order to fully understand the neurobiological mechanisms underlying language

processing as it relates to semantics, syntax, grammar, and ultimately conceptual thought, we first need to better understand how the building blocks of sentences and words (that is, phonemes) are processed.

In order to understand these hierarchically lower processes such as speech cue perception, we studied auditory brain ERPs, which supposedly reflect the basic auditory responses to speech sounds, with a sample of newborns. We assume that by using newborns as participants we could minimize the effect of linguistic experience in speech cue processing (see e.g. Turkewitz, 1988). Studying newborn infants provide also a possibility to study genetic influences of developmental language deficits. Dyslexia is assumed to be caused by both genetic and environmental factors (Pennington, 1990, 1991, 1995; Pennington and Smith, 1983, 1988). Genetic factors affect cognitive abilities throughout the life-span, and their effect is modified by environmental influences (Plomin, Owen, & McGuffin, 1994) in a way that the two are often impossible to differentiate from each other (Loehlin, 1989; Lykken, McGue, Tellegen, & Bouchard, 1992; Plomin, 1990; Plomin et al., 1994; Rose, 1995; Segal, 1993). Genetic factors can conceivably alter brain development through a large number of different pathways, and the parameters of brain structure and functional organization affected include such factors as neuronal number, neuronal migration, and axonal connectivity, which are determined or completed to a large extent before or by birth (Pennington, 1991). By using newborns as participants (minimizing the effects of the environmental factors) we could possibly see functional level differences affected by hereditary factors in the development of the brain between infants at risk for later language deficit and those without such risk.

There is a strong evidence that dyslexia has a genetic origin. For example, dyslexia has been shown to run in families (Gilger, Pennington, & DeFries, 1991; Vogler, DeFries, & Decker, 1985). Pennington (1995) concluded that these findings indicated strong evidence of *familiarity* of dyslexia: the median relative increase in risk to a child having an affected parent was about eight times the general population risk of five percent. However, according to Pennington (1990, 1995) this was necessary but never a sufficient condition for demonstrating the genetic influence: there should also

be evidence from *heritability*, *mode of transmission*, and *gene locations* in order to understand the more precise nature of the genetic influences in dyslexia[1].

As stated earlier, genetic influences can conceivably alter brain development (Pennington, 1991). In fact, there is substantial evidence in brain research studies that differences in neurological and anatomical structures and deviations from the normal pattern of functional properties (which, on the other hand, could be affected by genetic factors) play a role in decoding problems in developmental dyslexia (genetics-brain morphology-behavioral manifestations -linkage). The results from anatomical studies demonstrated certain morphological deviations such as neuronal ectopias and dysplasias in the brains of dyslexics (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Humphreys, Kaufmann, & Galaburda, 1990; Rosen, Sherman, & Galaburda, 1993). These anatomical studies also provided evidence for deviations from the standard pattern of cerebral asymmetry in the brains of dyslexics, especially in the planum temporale region. In vivo measurements such as MRI studies have confirmed these findings of structural differences (Flowers, 1993) and atypical patterns of cerebral lateralization (Hynd and Semrud-Clikeman, 1989; Jernigan, Hesselink, Sowell, & Tallal, 1991; Leonard et al., 1993). For example, there have been reports of altered hemisphere asymmetry of temporal lobes in a group of dyslexics (Dalby, Elbro, & Stodkilde-Jorgensen, 1998), and more specifically, altered asymmetry ($L \leq R$) of the planum temporale[2] in dyslexics (Galaburda, Corsiglia, Rosen, & Sherman, 1987; Hynd, Semrud-Clikeman, Lorys, Novey, & Eliopulos, 1990; Larsen, Höien, Lundberg, & Ödegaard, 1990). Galaburda, Menard, and Rosen (1994) provided further evidence of anatomical abnormalities in the auditory system,

[1] Heritability assumption of genetic influence in dyslexia has clearly been demonstrated by twin studies (DeFries, Fulker, & LaBuda, 1987; DeFries, Gillis, & Wadsworth, 1993; DeFries, Stevenson, & Gillis, 1991; Olson, Gillis, & Rack, 1991; Olson, Wise, Conners, Rack, & Fulker, 1989). Interestingly, in the study of Olson et al. (1989, 1991), deficits in phonological coding in dyslexics were more heritable than deficits in orthographic coding. Furthermore, there is evidence of autosomal dominant transmission in dyslexia (Lubs et al., 1993; Pennington, 1995), and preliminary results that chromosomes 15 and 6 may be linked to reading difficulties (Lubs et al., 1988; Pennington, 1991). There has also been evidence for a single autosomal gene (SPCH1 locus) involved in speech and language disorder (Fischer, Vargha-Khadem, Watkins, Monaco, & Pembrey, 1998).

[2] The linkage between the deviations in planum temporale asymmetry and deficits in dyslexia has been an especial subject of interest in dyslexia research. The planum temporale forms the superior posterior surface in the temporal lobe of the left hemisphere (Steinmetz and Galaburda, 1991). This brain location is essential for auditory comprehension (Schlosser, Aoyagi, Fulbright, Gore, & McCarthy, 1998). The planum temporale is a part of Wernicke's area, and the usual pattern of left greater than right planum asymmetry is thought to be a structural specialization that underlies the functional lateralization of certain language skills such as phonological processing to the left hemisphere (Pennington, 1991). According to Pennington (1991) this might explain the association of the altered planum temporale asymmetry with phonological coding deficits in dyslexics. The same kind of speculations that this altered asymmetry might produce complex qualitative alterations in the functional properties of the system has also been proposed by Galaburda et al. (1987).

which could be related to auditory processing deficits in dyslexics: the left side medial geniculate nuclei neurons of the thalamus (MGN, the subsystem which handles rapid temporal transitions) were significally smaller than the right in the dyslexic sample.

The association between functional deviations of the brain and altered cerebral processing of auditory stimuli in dyslexics has been studied, for example, by using regional cerebral blood flow (rCBF) and positron emission tomography (PET) methodologies (see e.g. Wood, Flowers, Buchsbaum, and Tallal, 1991). There have been reports of abnormal patterns of activation in the left temporoparietal regions during phonological processing (Paulesu et al., 1996; Rumsey et al., 1992), in the medial temporal regions during auditory perception tasks (Hagman et al., 1992), and in prefrontal and lingual regions during oral reading (Gross-Glenn et al., 1991) among dyslexic participants.

From this wide range of evidence it is reasonable to assume that there could also be differences in the electrical activity of the brain between dyslexics and normal controls. In other words, it is reasonable to assume that these probable differences can also be observed by using the event-related potential (ERP)[3] methodology. In fact, the ERP-technique has been widely used in the studies of different language related disorders like dyslexia (Brunswick and Rippon, 1994; Byring and Järvilehto, 1985; Chayo-Dichy, Ostrosky-Solis, Meneses, Harmony, & Guevara, 1990; Chayo-Dichy, Ostrosky-Solis, Meneses, Harmony, & Miguel, 1991; Jirsa, 1992; Kraus et al., 1996; Mason and Mellor, 1984; McAnally and Stein, 1997; Otto et al., 1984; Pinkerton, Watson, & McCelland, 1989; Segalowitz, Wagner, & Menna, 1992; Shucard,

[3] Event-related potentials can be recorded from the brain regions that are activated by the stimulation in each sensory modality (e.g. visual, auditory, somatosensory, and motor readiness potentials). In this study we are interested in auditory evoked potentials, and more specifically in late cortical auditory potentials. For a description of brainstem and middle latency auditory evoked potentials, see e.g. Eggermont (1985, 1992). The ERPs can be characterized as a series of positive and negative deflections which are thought to result from the volume-conducted electrical activity generated in various brain regions (van Boxtel, 1998). The ERP components are usually could be categorized into exogenous and endogenous components according to their relations to extrinsic and intrinsic stimuli to the nervous system (Näätänen, 1992). The exogenous components occur near the eliciting event, and the characteristics of the components depends on the physical parameters of the eliciting stimulus (Kramer, 1985). The endogenous components, however, are "invoked" by the psychological demands of the situation rather than just by the stimulus parameters (Donchin et al., 1978). Along with this exogenous-endogenous classification there has also been suggestions for more specific categorization (Näätänen, 1989). According to some authors the theoretical definition of the ERP components is based on these underlying neuronal generators, which are identified by the scalp distribution (Näätänen and Picton, 1987; Sams, Alho, & Näätänen, 1984), the polarity, the amplitude, and the latency (Donchin et al., 1978) of these distinct physiological units. But as noted, for example, by Donchin et al. (1978), this definition must also be based on the function of the ERPs, that is, on the relation with experimentally induced variations in determining the subprocesses. With the ERP technique it is possible to obtain knowledge both from the end-product of the processing as well as from the sequence, the timing and the stages of the specific processes (Leppänen and Lyytinen, 1997). ERPs could also be used as a differentiating measure of different cognitive processes (Connolly at al., 1992; Gevins and Cutillo, 1986; Rösler et al., 1986).

Cummins, & McGee, 1984; Stelmack, Rourke, & van der Vlugt, 1995; Taylor and Keenan, 1990). ERPs have also been used to differentiate between various types of dyslexia subgroups (Aylward, 1984; Dool, Stelmack, & Rourke, 1993; Duffy, Denckla, McAnulty, & Holmes, 1988; Duffy and McAnulty, 1990; Fried, Tanguay, Boder, Doubleday, Greensite, 1981). Auditory ERP measures as assessment tools of developmental language related disorders have been reviewed, for example, by Leppänen and Lyytinen (1997), Ollo and Squires (1986), and Rosenthal, Boden, and Callaway (1982).

However, from our point of view the most interesting aspects of ERP and dyslexia studies concerns the results obtained from infants, and especially from newborns[4] with a genetic risk for dyslexia (for a review of using ERPs in populations at genetic risk, see Friedman, 1990). Leppänen, Pihko, Eklund, and Lyytinen (1999, in press) and Pihko et al. (1999, in press) studied other subsamples of newborns who participated in this longitudinal JLD-project. Pihko et al. (1999, in press) studied whether the ERPs to stimuli differing in vowel duration (/ka/ versus /kaa/) would differ between at-risk and control infants. There were no major stimulus or group effects found in this study of newborns, but at the age of six months significant group effects (in the response to the standard /kaa/) were observed. However, in the study of Leppänen et al. (1999, in press) the longer interstimulus interval (ISI) was used in order to test if the slower presentation rate would lead to an enhancement of the brain's response to change in stimulus duration (/ka/ versus /kaa/) in newborns. There were significant stimulus and stimulus rate (slow rate condition) effects which occurred more consistently in the left hemisphere in the control group, while in the at-risk group they occurred in the right

[4] When studying ERPs to auditory presented stimuli in newborns it is important to consider the maturational and developmental aspects of ERPs. The developmental trends in ERPs can be seen, for example, in systematic progression from a predominantly negative to a predominantly positive ERP waveform during the preterm period (Kurtzberg, Hilpert, Kruezer, & Vaughan, 1984; Novak, Kurtzberg, Kreuzer, & Vaughan, 1989). Pihko et al. (1999, in press) reported also ERP changes from a slow positive deflection in newborns to a more differentiated negative-positive-negative waveform in 6-mont-olds. When comparing ERPs from young infants to those measured from older children and adults certain developmental changes can be found such as the increase in morphological complexity, increase of the amplitude, and the decrease in component latency (Thomas and Crow, 1994, see also Shucard, Schucard, and Thomas, 1987, 1988). But it should be noted that comparison between the ERP components of different age groups may be difficult to interpret, because the ERP components have complex maturational timetables, and they differ from each other in terms of age of emergence, ERP waveform, latency, amplitude and task conditions generating these components (Courchesne, 1983, 1990). Furthermore, knowledge of the developmental stage of one ERP component may not accurately predict the stage of development of another, and the exact rate of development may vary from infant to infant (Anthony and Friedman, 1991; Courchesne, 1990; Friedman, 1991; Thomas et al., 1997). Age-related changes may reflect cognitive growth, brain maturation, or the developmental time course of their interaction (van der Molen and Molenaar, 1994). And as further stated by van der Molen and Molenaar (1994), it is problematic to attribute age-related changes in ERP to cognitive development without examining the sensitivity of this measure to variations in task demands on the information-processing system.

hemisphere. These group differences showed that the brain of infants at risk for familial and developmental dyslexia process speech/auditory stimulus durations differently from infants without such a risk, even from birth. The differences between at-risk and control groups were also obtained in the study of Leppänen et al. (1999, submitted) with six-month-olds. They examined whether the groups differed in their ERPs to a duration change of the stop consonant (/ata/ versus /atta/), and found that these groups differed both in their exogenous responsiveness and in their responses to stimulus duration change (see also Richardson, 1998). Leppänen at al. (1999, submitted) concluded that these results are in line with the suggested timing deficit as a potential underlying factor for future problems in learning to efficiently manipulate sublexical units during reading acquisition (see also Fitch et al. 1997, Frith and Frith, 1996, Tallal, 1980, 1984)[5].

The results from the studies of Leppänen et al. (1999, in press, 1999, submitted) demonstrated that the brain electrical activation generated by speech sounds varying in their temporal structure (/ka/ versus /kaa/, /ata/ versus /atta/) differed between the at-risk and control groups. We wanted to investigate with the other subsample of newborns if we could find differences in the ERPs between groups by using stimuli which varied according to their place of articulation clues (/ba/, /da/, /ga/, /paa/, /taa/, /kaa/, respectively). These complex and rapidly changing acoustic temporal and spectral characteristics of speech signal in a brief time window are critical cues for stop consonant identification (Fitch et al., 1997). As stated by Tallal (1980), the problems among older dyslexics in tasks such as stop consonant identification are thought to arise from nonlinguistic difficulty in the processing of the brief formant transitions in consonant stimuli (e.g. cues that differentiate /ba/ from /da/, and /da/ from /ga/). ERPs have been proved to be a reliable method for differentiation of these rapidly changing acoustic speech cues between consonants (Dhaene-Lambertz and

[5] This hypothesis of general temporal processing deficit in dyslexia research has also been confirmed not only in the auditory modality (Farmer and Klein, 1995; Hari and Kiesilä, 1996; Johnsrude, Zatorre, Milner, & Evans, 1997; Klein and Farmer, 1995; Reed, 1989), but also in the visual modality (Frith and Frith, 1996; Lovegrove, 1993; Stein and Walsh, 1997). It should be noted, however, that some criticism has been directed against this hypothesis of temporal processing deficit (Brady, 1997; de Gelder and Vroomen, 1998; Mody, Studdert-Kennedy, & Brady; Rayner, Pollatsek, & Bilsky, 1995; Studdert-Kennedy and Mody, 1995). The discrepancies between results and conclusions derived from studies which have emphasized the critical role of acoustic versus phonological deficits could be explained by the fact that it is unlikely that any single causal factor underlies all patterns of language deficits (Manis et al., 1997; Martin, 1995). Furthermore, it is known that the manifestation of these language problems changes due to linguistic experience and compensatory strategies (Steffens, Eilers, Gross-Glenn, & Jallad, 1992). The issue is further complicated by the possibility that language impairments are likely to vary according to the criteria used to classify reading disabilities (Scarborough, 1990).

Dehaene, 1994; Kraus et al., 1993; Kraus, McKee, Sharma, Carrell, & Nicol, 1992; Maiste, Wiens, Hunt, Scherg, & Picton, 1995; Sharma, Kraus, McGee, Carrell, & Nicol, 1993). The use of ERPs was also argued for the fact that this methodology has been shown to differentiate between dyslexics and controls, even at the early states of development (see earlier). Furthermore, with the ERP-technique it is possible to avoid some methodological difficulties usually met in studies with newborns and infants. Because the procedure does not necessarily require the subjects' conscious attention (Näätänen, 1992), measurement can be performed, for example, while subjects are at sleep (Leppänen et al., 1997; Duclaux, Challamel, Collet, Roullet-Solignac, 1991), as was the case in our study.

The studies of Molfese et al. have been one of the starting points for this study. In the different studies of Molfese et al. they have used the ERP methodology in investigations of the newborns' differentiation of speech sounds using synthesized stop consonant-vowel syllables which differed according to place of articulation (e.g. /ba/, /da/, and /ga/) and/or voice onset time (e.g. /ba/-/pa/, /da/-/ta/, /ga/-/ka/). In most of the studies of Molfese et al. there were also nonspeech versions of these stimuli (for example, nonphonetic transitions).

Behavioral studies (for example, using dichotic listening method) and clinical evidence from neurologically impaired populations have provided evidence that speech and language functions are primarily lateralized in the left hemisphere in adults (Bryden, 1982), in children (Hiscock, 1988), and in young infants (Segalowitz, 1983; Witelson, 1987). The evidence from behavioral studies (Bryden, 1988; Obrzut, 1988) and from anatomical and functional brain research (see earlier) has also shown that deviations from normal hemispheric asymmetry are related to language difficulties such as dyslexia. Molfese et al investigated if the lateralization of language functions to left hemisphere could be found to occur prior to the time of language acquisition (Molfese, Freeman, & Palermo, 1975; Molfese, Nunez, Seibert, & Ramanaiah, 1976). Molfese et al. also extended their studies to investigate what those stimulus characteristics are that elicit these lateralized responses (Molfese and Molfese, 1979a, 1979b, 1980). The study of lateralized responses also extended to attempts to predict later language development (Molfese and Molfese, 1985, 1997; Molfese and Searock,

1986). For reviews of the results from these studies, see Molfese (1987), Molfese and Bentz (1988), Molfese and Molfese (1986, 1994), Molfese and Narter (1997), Simos and Molfese (1997), and Simos, Molfese, and Brenden (1997). The results concerning newborn ERPs predictive value is of most interest from our starting-point.

Molfese and Molfese (1979a) investigated the differentiation of speech sounds varying in terms of second formant transitions (consonants heard as /b/ versus /g/). The data was analyzed by the principal component analysis (PCA) and variance analysis -techniques. In PCA, the factor analysis procedure is used in order to identify the latencies or timepoints of ERPs that varied the most across subjects and experimental conditions. The factor scores extracted by PCA were further analyzed by the ANOVA program in order to investigate from which experimental conditions the variability originated. For Factor 4 (between 128-272 ms, peak at 192 ms), there was an asymmetric response that was characterized by the left hemisphere's ability to differentiate between the consonants that contained a normal formant structure. The authors concluded that the early laterality effects were due to the presence of mechanisms within the left hemisphere that could detect and analyse specific acoustic cues common to the speech signal. There was also a later (Factor 3, between 490-704 ms, peak at 630 ms) bilateral response that could also differentiate these normal formant structure consonants.

Molfese and Molfese (1985) further investigated the role of early lateralized processes as a means to predict future language development. They could identify specific ERP components that discriminated between groups of children who appear to have different levels of language skills at the age of three years (McCarthy verbal scores). The ERPs recorded from the left hemisphere of the high performance group varied systematically as a function of consonant sound with speech formant structure (Factor 3). The peak was smaller between 88 and 240 ms for the /b/ initial syllables than for the /g/ syllables. This pattern of response in the high group was similar to the results in the study of Molfese and Molfese (1979a) for Factor 4 (128-272 ms), and in the study of Molfese, Burger-Judisch, and Hans (1991) for Factor 3 (80-330 ms, in which differences were clearest in the left parietal and frontal areas.).

A second ERP component (Factor 7 with a late peak latency of 664 ms) also discriminated between the high and low group in the differentiation of consonant sounds as a function of the vowel /i/. This component reflected bilateral activity. This pattern was similar to the findings of Molfese and Molfese (1979a) for Factor 3 (490-704 ms), and Molfese et al. (1991) for Factor 1 (520-700 ms, with the exception that this effect occurred only in the left hemisphere). In other words, there were clear similarities related to consonant differentiation between these three aforementioned studies: the effect of the initial ERP only components occurred over the left hemisphere, it was within the same temporal region of the waveforms, and differentiated the same phonetic categories even though other acoustic cues differed between these studies. The later component, which was within the same temporal region of the waveforms between studies, also reflected consonant differentiation related effects.

These results of Molfese and Molfese (1985) indicate that the sensitivity to specific language related cues seems to relate clearly to later language development: the high performance group not only differentiated between consonants alone and consonants in different vowel environments, but also between variants of the speech and nonspeech stimuli. Molfese (1989) provided further support for the findings with a different sample of newborns: Discriminant function classified correctly 68.6 % of the newborn ERPs from the children with McCarthy scores above 50 and 69.7 % of those with scores below 50 at three years age. Molfese and Molfese (1997) extended this language performance prediction from newborn ERPs to five years of age. Factors 2 and 6 (between 170-320 ms, and between 70-140 ms, respectively, matching the latency of factors identified in 1985) were used in discriminant function analyses to distinguish infants based on test scores (verbal subtest of Stanford-Binet). The accuracy of classification ranged from 78.9% to 95.8%. In general, the ERP amplitude, positive in polarity, was larger in the high performance group.

These results indicate that newborn ERPs can be used in predicting later developing language skills. Although different language performance tests (McCarthy verbal scores and Stanford Binet) were used at different ages (three and five years),

discrimination between the high and low groups could be made[6]. The authors suggested that nervous systems of the high performance group in these studies could be either more sensitive to or could make finer differentiations between a variety of auditory events that share some commonality with speech perception events. They further stated that the earlier an infant can detect and discriminate between patterns of sounds in their language environment, the better able that infant will be to utilize such information as the extensive process of language acquisition begins: the accuracy of the perceptual mechanisms creates a base for later language and cognitive processes (Molfese and Molfese, 1985, 1997; Molfese and Searock, 1986). As related more specifically to dyslexia research, children who do not perceive clear distinctions between phonemes may not form readily accessible long-term memory representations of these phonemes, and this would lead to difficulties in segmenting and manipulating phonemes, and in learning grapheme-phoneme mappings (Manis et al., 1997). The results of Molfese et al. showed that ERP measured at birth could also be used in early identification of infants with the risk for later cognitive problems, which, on the other hand, would help earlier and more effective intervention in such problems.

We were primarily interested in the newborns' ability to detect brief formant transitions which differentiate consonants from each other. We used the same synthetic consonant-vowel syllables (/ba/, /da/, /ga/) as Molfese et al. in their studies. We wanted to compare if the factors which differentiated consonants in our study could be placed in the same latencies as the corresponding factors in the studies of Molfese et al. More specifically, we were interested if an early component between 90-300 ms could be found, which would reflect the consonant differentiation qualities of the left hemisphere. Furthermore, we were interested in whether there would be a later bilateral component around 500-700 ms, which would also reflect consonant differentiation related effects. Because the participants in the studies of Molfese et al. were healthy newborns without any kind of risk for later language disorders, only the control group from our sample were included in this first stage of analyses. We

[6] These findings apply to consonant-vowel environments, in other words, to the differentiation of the place of articulation cues at birth, but Molfese and Searock (1986) demonstrated that brain responses of one-year-old infants to vowel sounds, in other words, to voice onset time cues could also differentiate language performance later in life.

extended the study of newborn speech cue processing and included also natural stimuli (/paa/, /taa/, /kaa/) under investigation.

The most interesting results from these studies of Molfese et al., however, concerned the predictive value of newborn ERPs. As noted earlier, in these studies Molfese et al. used healthy newborns as participants. We also had a group of newborns that had a genetic risk for the later language deficits. Molfese et al. showed that ERP differences were related to later language difficulties, which makes possible to hypothesize that these the differences might also be seen between the at-risk and control group in our study. We examine whether there are differences in ERP responses to various consonants between the at-risk and control group, in other words, whether the speech sound processing of newborns with a genetic risk for later language problems is differt from that of newborns without such a risk. More specifically, according to the results of Molfese et al. these differences should be clearest between 90-300 ms in the left hemisphere and between 500-700 ms in both hemispheres. Based on the results from studies of Molfese et al. we hypothesize that especially the differentiation between /b/ and /g/ differentiates the groups. Finally, we investigated in which brain locations these differences are located and which brain areas are differentially active.

2. METHODS

2.1. Participants

Forty-nine newborn infants were included in this study. Of these 26 infants (16 males and 10 females) belonged in the at-risk group, and 23 participants (13 males, 10 females) in the matched control group. Originally, the ERPs of 75 newborns were recorded, but the data from 26 participants were excluded because no data could be obtained, or not enough artifact-free data could be collected during quiet sleep.

In the control group, the participants had a mean gestational age (GA) of 40.1 weeks (SD = 1.0, range: 38.5 - 42.1 weeks) and a mean birth weight of 3688.3 g (SD = 535.1, range: 2730 - 4500 g). One-min. and 5-min. Apgar scores averaged 9 and 9.05 (SD = .447 and .498, respectively). The participants were tested within 33 - 149 hr (1-6 days) from birth[7]. Thus the mean conceptional age (CA) at the time of measurement was 40.6 weeks (SD = .998, range: 38.5-42.1).

In the at-risk group, the participants had a mean gestational age (GA) of 40.0 weeks (SD = 1.6, range: 36.9 - 43 weeks) and a mean birth weight of 3659.8 g (SD = 508.5, range: 2970 - 4600 g). One- min. and 5-min. Apgar scores averaged 8.54 and 8.92 (SD = 1.24 and .935, respectively). The participants were tested within 36 - 175 hr (1 - 7 days) from birth, except for 4 participants whose GA were below 38 weeks. They were tested at about 40 weeks postconceptual age (within 14 - 23 days from birth). Thus the mean conceptional age (CA) at the time of measurement was 40.8 weeks (SD = 1.1, range: 39.0 - 43.8).

[7] The reason for not measuring the newborns immediately after birth was the fact that auditory acuity improves as a result of the draining of amniotic fluid from the middle ear within the first days of life (Spreen, Risser, & Edgell, 1995).

There were no significant differences between the control and risk group in gestational age, $F(1, 45) = .16$, $p > .692$; in birth weight, $F(1, 45) = .23$, $p > .636$; or in 1 and 5 min. Apgar scores, $F(1, 45) = 2.62$, $p > .112$ and $F(1, 45) = .30$, $p > .585$, respectively.

2.2. Stimuli

The stimuli were synthetic stop consonant-vowel syllables (/ba/, /da/, /ga/). The five-formant synthetic CV syllables were obtained from D. Molfese. Technical information for /ba/, /da/ and /ga/ is found in the article of Molfese and Molfese (1997), and Stevens and Blumstein (1978). These stimuli were previously identified by adult participants as members of their respective categories (Stevens and Blumstein, 1978). These stimuli were originally synthesized on a Klatt cascade synthesizer so that amplitudes of the individual formants were modulated as a function of the respective formant frequencies as in natural speech (Molfese and Molfese, 1997; Stevens and Blumstein, 1978). The central frequencies of the steady-state portion of the formants were constant across the different consonant sounds. The duration of the F1 formant transition varied between 15 and 45 ms as a function of the initial consonant sound. The transition duration for all other formants was fixed at 40 ms, and the voicing duration was 250 ms.

In the stimuli set there were also naturally recorded /paa/, /taa/, /kaa/, and /ka/. The shorter syllable /ka/ was included in the procedure in order to compare ERP components between this equal probability and oddball-paradigm[8]presented to the same participants. However, responses to /ka/ were not included in the analyses presented in this study. The total duration of the natural stimuli was also 250 ms (except /ka/ 110 ms).

[8]In addition to this equal probability paradigm reported here, the differentiation of change in vowel duration was also studied with these same newborns (see Leppänen et al., 1999, in press, and Pihko et al., 1999, in press) using MMN paradigm (Näätänen and Alho, 1995; Kraus, McGee, Carrell, and Sharma, 1995).

As described by Borden and Harris (1981), these stimuli which differed according to their place of articulation can be categorized as labials/frontal (/p/,/b/), alveolar/middle (/t/,/d/), and palatal-velars/back (/k/,/g/). The cues indicating place of articulation of a stop consonant include the frequency position of the burst in relation to the vowel, and the formant transition, especially F2 (for example, the stimuli heard as /ba/ have most sharply rising transitions, /da/ less sharp or even falling transitions, and /ga/ falling transitions in the transition continuum), and the frequency of the noise components (Borden and Harris, 1981).

The intensity of the stimuli was 75 dB SPL, calibrated before the experiments using the Brüel and Kjaer precision sound level-meter (Type 2235). The stimuli were presented in separate blocks, comprising 20 presentations of each syllable (the number of blocks ranged from 1.5 to 5 for each participant). The inter-stimulus-interval (onset to onset) ranged randomly from 3910 to 7285 ms in order to reduce habituation and expectancy effects[9]. The stimuli were presented with equal probability and in pseudorandom order (equal probability -paradigm), with the exception that the same sound did not appear three times or more in a row.

2.3. Procedure

The experiments were conducted at the neurophysiological laboratory of the Central Hospital of Central Finland in Jyväskylä. The parents were invited to observe the experiments if they wished. The experiments were conducted in a dimly lit EEG-laboratory room. The infants were lying in a slightly reclined position (5.3°) in a crib designed for the purpose, in which the mobility of the infant's head was minimized by a small pillow. The auditory stimuli were delivered through a loudspeaker located at the foot of the crib 39 cm above the bed level and 60 cm from the estimated head

[9] This kind of rare or improbable stimuli has been shown to elicit larger amplitudes in newborns (Tokioka, Pearce, & Crowell, 1995). Slower presentation rate of the stimuli has also been shown to lead to enhancement of the brain's response to stimuli, and furthermore, make ERP differences between the at-risk and control groups more marked in the other subsample of newborns who participated in the JLD-project (Leppänen et al., 1999, in press).

position of the infant (the angle between the loudspeaker-head line and bed level was 41°). The recordings were suspended when the infant was either crying or moving excessively.

The EEG was recorded using disposable Ag/AgCl-electrodes (Blue sensor, Medicotest, Denmark), which were attached to the frontal (F3, F4), temporal (T3, T4), central (C3, C4), and parietal (P3, P4) scalp sites, according to the International 10-20 electrode system. These EEG electrodes were referred to the ipsilateral mastoid, except T3 and T4. All of the electrodes were referred to the corresponding electrode site over the opposite hemisphere (bipolar derivations). However, only the data from monopolar derivations are reported here[10]. The electrooculogram (EOG) was recorded with two electrodes, one slightly above and lateral to the left eye and the other below the right eye. These EOG electrodes were referred to the left mastoid. A ground electrode was placed on the forehead. ECI Electro-Gel (Electro-Cap International, Inc., Eaton, USA) was used as an electrolyte. The electrical resistance or impedance of the electrodes before measurement was < 10 kiloohms (kΩ), except for five participants where the impedance of the single channel exceeded 10 kΩ.

The EEG was recorded and signals were amplified by Nihon Kohden Neurofax EEG-5414K. The EEG-epochs were recorded in the timewindow from 950 ms before to 950 ms after stimulus presentation, and were stored at the temporal sampling rate of 200 Hz.[11] The time constant was 0.3 and the high frequency filter was 35 Hz. AC-filtering was on.

[10] Monopolar recordings emphasize global effects and accurately demonstrate waveforms, but may not easily localize spatially restricted findings, whereas bipolar recordings are best for localization but may distort the morphologies of ongoing EEG transients and are less sensitive to global events (Duffy, 1994). The evaluation of the reference electrode sites has been discussed, for example, by Wolpaw and Wood (1982).

[11] This was determined using a rate greater than twice the highest frequency in the input signal (the "Nyquist frequency"), and even if little information is seen in EEG above 20 Hz, there are muscle artifact that usually exceed 100 Hz (Duffy, 1994). Failures in sampling at a sufficiently high frequency induce "aliashing", in which signal frequencies above the sampling rate appear artificially folded down (Duffy, 1994).

2.4. Analysis of the ERP data

2.4.1. The sleep state classification.

The sleep stages have a considerable influence on cortical auditory responses (Duclaux et al., 1991). For this reasonthe sleep stages were controlled by classifying the EEG-epochs into four categories according to the infants' sleep states (wakefulness, active sleep, quiet sleep, or indeterminate state). The states were defined according to behavioral criteria defined in the sleep-state scoring manual by Anders, Embde, and Parmalee (1971). In addition, eye movements were monitored at the EOG-channels from the ongoing EEG. Each 1-min. period of the measurement was classified as one of the states. The behavior of the infant was observed and coded on-line during the assessment for the classification of the sleep states, which was done off-line after the measurement. The procedure was the same as in the study reported by Leppänen, Eklund, and Lyytinen (1997), where the interrater agreement of the on-line-coding of the infant's behavior (eyes open or closed, facial or body movements, crying, etc.) between two independent observers was 95 %. This was calculated from the data of five randomly chosen participants and was defined as the percentage of the total number of EEG-epochs that the two observers agreed upon. The comparable interrater agreement of the classification of the EEG-epochs into four sleep states was 92 %. Only the data classified as quiet sleep are reported here[12].

2.4.2. ERP-averaging

The time window used for ERP-averaging[13] was -50-950 ms (with the -50 ms prestimulus baseline). The ERP-data averaged across each collected datapoint (one in

[12] In quiet sleep, the newborns' breathing and pulse is slow and regular, and movements appear only occasionally, except that quiet sleep might be startle responses, which appear as massive, spasmodic jerks of the entire body, followed by bouts of disturbed breathing and a pounding heartbeat (Maurer and Maurer, 1988).

[13] By averaging multiple EEG-epochs it is possible to get a synchronized ERP pattern that is time-locked to a certain stimulus event or a meaningful task event in the subject's environment (Donchin, Ritter, & McCallum, 1978). The averaging cancels spontaneous and random EEG activity in relation to the stimulus, and thereby brings out the waveform that is invariant across the stimulus presentations (Coles, Gratton, & Fabiani, 1990). By using this averaging procedure the following assumptions must be met: the components must be temporally invariant over the repeated presentations of the stimulus; the morphological characteristics of the component must be invariant over the trials; and the background noise (the spontaneous EEG) must not be systematically related to the components (Kramer, 1985).

five ms) resulting in 190 datapoints for each averaged response. EEG-epochs which contained excessive eye movements, defined as the EOG deflections exceeding +/- 150 microvolts (μV), and muscle activity or other extra-cerebral artifacts, defined as the EEG deflections exceeding +/-200 μV, during the time window were excluded from averaging[14]. With this criterion, the percentage of epochs rejected was 42.81 %. In order to be included in averaging and further analysis, at least 16 acceptable EEG-epochs (trials) for each stimulus type were required (mean number of accepted trials was 38, range 16 - 65).

2.4.3. Principal component analyses

The averaged ERP-responses were divided to two different sets; in other words, responses to natural and synthetic sounds, because of the different structure of these stimuli. These responses were used as input to two separate factorial principal component analyses (PCA)[15].

ERP data may be considered as the sum of independent components, and principal component analysis (PCA) can be used to extract such underlying components (Skrandies, 1989). PCA reduces the considerable amount of data collected in ERP-measurements by finding a set of non-redundant waveform descriptors that explain most of the variance in the original data (Skrandies, 1989). This is how PCA describes the complex relations between a large number of original variables in a more manageable manner (van Boxtel, 1998). Principal component analysis identifies the latencies or time points of ERPs that varied the most across experimental variables. Time points, which in our study were selected every 10 ms of each averaged ERP,

[14] The used EOG / EEG criteria were chosen after testing and comparing of three different alternatives. The data of eight randomly chosen participants were averaged using EOG/EEG criteria of +/- 150 /200, +/- 100/150, and +/- 150/100 microvolts. The last criterion was too strict, especially concerning the EEG. In the selection between the two first, the +/- 150/200 criterion was more suitable, because the remaining number of trials were larger (in other words the signal-to-noise ratio were better). Furthermore, when empirically tested by two tailed *t*-test there nevertheless were no differences in grand averages between these two excluding criteria ($p > .05$).

[15] In summary, PCA represents the data in a concise, parsimonious way; it determines ERP components from the data without assuring in advance any particular waveforms for the components; it extracts components which are independent of each other; it measures the amounts (contributions) of various components in observed ERPs; uses measures that have greater reliability than measures at any single time point or peak; and it identifies and measures components that overlap in time (Chapman and McCrary, 1995). The extracted principal components are closely related to the original variables: they are simply weighted linear combinations of all the original dependent variables (van Boxtel, 1998). In other words, principal component analysis does not create effects that are not in the data (Chapman and McCrary, 1995).

served as the variables: that is there were 95 dependent variables. The ERP averages recorded from the different electrode locations, hemispheres, experimental conditions and participants were treated as the cases or observations. In other words, there were 414 cases, when only the control group was included in analysis (3 x 2 x 3 x 23), and 882 cases when both groups were included (3 x 2 x 3 x 49)[16].

The principal components (PCs) or factors were extracted from the data in a hierarchical manner: the first factor accounts for the largest proportion of the total variance in the data. The following factors are both orthogonal to the preceding ones, and they account for the largest residual variance (van Boxtel, 1998). The number of factors included in the final analyses depended on the magnitude of factor loading and amount of variability each factor could account for[17].

At first, PCA computed a correlation matrix between all individual time points (variables)[18]. For the next step, the initial matrix was rotated using the normalized varimax criterion in order to improve factor distinctions while preserving the orthogonality of PC scores (Chapman and McCrary, 1995)[19]. After rotation, the PCA assigned *factor loadings and scores.* As described, for example, by van Boxtel (1998) *factor loadings* represent the systematic contribution of each component to the voltage at each time point (indicating the instants in the ERP in which amplitude variability exists). *Factor scores*, however, represent the contribution of each component to each individual ERP waveforms (indicating the nature of the variability). These scores

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[16] The number of cases must be approximately five times the number of variables in order to produce a statistically reliable PCA solution (Hunt, 1985), and in order to reduce the likelihood that the results are based on sample specific findings (Roemer, Josianssen, & Shagass, 1990). In our study, the ratio between cases and variables comes up to these requirement.

[17] Bartlett's test of sphericity (*ps* < .000, correlation matrix is not an identity matrix) and Kaiser-Meyer-Olkin measure of sampling adequacy (>.880) showed that the basic assumptions concerning the factorial model were fulfilled.

[18] This analysis computes the correlations across all ERPs in the data set, with the crucial consideration that time points (variables) that are correlated belong to the same underlying component (Chapman and McCrary, 1995). The mean of each variable is subtracted from the values of the variable (that is, from each case), and the resulting differences are divided by the standard deviation of the variable: this how all variables have equal variance; in other words, they were standardised (Donchin and Heffley, 1978; van Boxtel, 1998). After these transformations the cross products are computed by summing the results of the multiplication of all possible pairs of variables across cases. Analysis of the correlation matrix leads to the extraction of principal components that correspond to the variance (scaled by the standard deviations) around the grand mean ERP. In other words, by using the correlation association matrix, a portion of the variance, which was originated from differences between the variances of individual variables, was removed (Donchin and Heffley, 1978).

[19] By rotating, the matrix is transformed into one that has a simpler structure, and that is easier to interpret (van Boxtel, 1998). A single variable has a high loading on only one component and zero or negligible loading on all other components, which means that the temporal overlap of the principal components is minimized (Chapman and McCrary, 1995; van Boxtel, 1998). For a discussion of the usefulness of rotating, see Rösler and Manzey (1981) and Wastell (1981a).

represented the factors in further analysis of variance, which indicated whether the factor scores (the region of the variability in the ERP identified by PCA) either systematically increased or decreased in size relative to some experimental conditions (van Boxtel, 1998). In this study, the factor loadings greater than .4 were used to identify the region of variability in each of the factors.

2.4.4. Further analysis

The factor scores extracted from principal component analysis were treated as an input for a series of multivariate and univariate analyses of variance (MANOVA/ANOVA) for repeated measures[20]. These scores indicate whether the region of variability in the AER identified by the PCA changes systematically as a function of the experimental conditions. The experimental conditions varied according to three consonants (/b/, /g/, /d/ in synthetic stimuli; or /p/, /t/, /k/ in natural stimuli), three electrode locations (frontal, central, and parietal), and two hemispheres (left, and right, that is the electrode locations were F3, F4, C3, C4, P3, and P4). In other words, there were 18 dependent variables in these analyses. Again, the natural and synthetic sets were treated separately, and in both sets the analyses were performed in each component separately.

When the significant MANOVA/ANOVA had been found, the next step was the follow-up analyses using multivariate difference contrasts. It should be noted, that the MANOVA/ANOVA analyses, as well as follow-up multivariate contrast analyses, were based on the factor scores obtained from PCA, in other words, the obtained interactions could not directly be referred to the original ERP latency, amplitude, or polarity differences. The mean factor scores were used in the interpreting of the MANOVA/ANOVA interactions. In the group comparisons (when possible effects was due to group differences) the MANOVA/ANOVA analyses was made based on

[20] By MANOVA it is possible to evaluate mean differences on these dependent criterion variables simultaneously, and consider the relationship or correlations (direction and the magnitude of correlations) between the variables (Bray and Maxwell, 1985). Furthermore, repeated measures designs are required for these kinds of ERP experiments because the comparisons are made within subjects and across experimental conditions. That is, each participant is being measured multiple times on the same dependent variable (O'Brien and Kaiser, 1985). A primary advantage is that this procedure controls for individual differences (Bray and Maxwell, 1985). The use of MANOVA approach to repeated measures design was chosen because it does not make the assumption of sphericity, and thus offers several advantages over the traditional univariate approach (Vasey and Thayer, 1987).

the factor scores of the both groups extracted in the same PCA procedure[21]. In the group comparisons, discriminant function analysis was also used to assess how accurately newborn ERP could be used as a classifying measure.

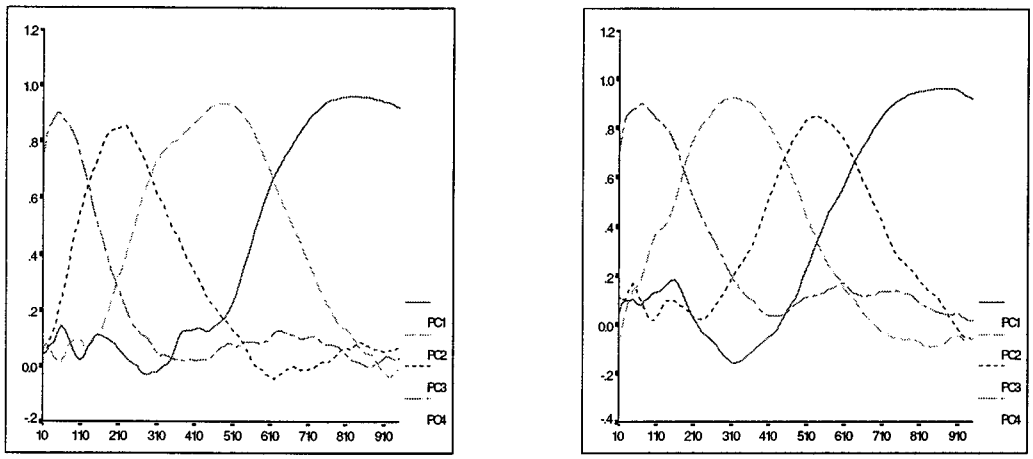
[21] In these kind of group comparisons there are two possibilities, namely analyzing both groups together in the same PCA or using separate PCAs in different groups. According to Hunt (1985) including subjects from heterogeneous groups to the same PCA could violate the normality assumptions (the amplitude of the factor scores are distributed normally across records). But as stated by Roemer et al. (1990), the decision between analyzing all groups together or in separate PCAs should be made according to the relatedness of these subsamples: if there is evidence of a high degree of relation between the sets of basis waves and thus the two sets of factor scores, the combining of the subsamples is a valid solution. In our study, the group comparisons we analyzed using same PCA. This decision was made because the groups were not too heterogeneous from each other. Furthermore, in MANOVA the normality of the variables was tested by the Kolmogorov-Smirnov-test, which showed that variables were normally distributed ($p > .05$), in other words the normality assumptions were not violated. In the case of group comparisons, the Box's M tests were used to verify if the variance-covariance matrices were equal in both groups. In the first and second factors of the synthetic stimuli set there were slight deviations from the equality ($p < .021$ for Factor 1, and $p < .039$ for Factor 2). But as stated by Olson (1974), Box's M test is generally not useful, because the test itself is extremely sensitive to departures from normality. Furthermore, as stated by Bray and Maxwell (1985), it is unlikely that all of the assumptions will be met precisely, and MANOVA is relatively robust to these kinds of violations. The possible lack of sphericity, in other words the assumption that the variance of the differences between pairs of levels of a factor would not be equivalent for all pairings of a level (Garnsey, 1993), was compensated by using Greenhouse-Geisser corrections in order to avoid type I errors. And as stated earlier, this possible lack of sphericity is also circumvented by using the MANOVA approach.

3. RESULTS

In general, the ERPs recorded both from the risk and control group in synthetic stimuli set were characterized by an initial small positive-negative deflection at 110 ms, a major positive deflection reaching its maximum around 300 ms, and a later occurring slow ongoing negative deflection which increased to the end of the recording window (maximum negativity around 800-950 ms, see Figures 2a, and 3a). The responses to natural stimuli (/paa/, /taa/, /kaa/) in our study were similar to the responses of synthetic stimuli, except that the positivity at around 300 ms was larger in amplitude (see Figures 2b, and 3b).

3.1. Control group

For the first step, only the participants of the control group were included in analyses for normative ERPs generated by speech sounds in newborns. For the ERP data generated by the synthetic stimulus set, four principal components (PCs) or factors accounted for 89.1 % of the total variance. The timewindow for a factor was determined as the latency range at which the factor loadings for a given factor exceeded .4. For example, Factor 1, which accounted for 31.8 % of the total variance, occurred at the timewindow of 555-950 ms, reaching the maximum factor loading at 825 ms. For the ERP data generated by the natural stimuli set there were 4 factors, respectively, which accounted for 89.5 % of the total variance. The factor loadings are presented in Fig. 1a (factors from the synthetic stimuli set), and in Fig. 1b (factors from the natural stimuli set, respectively). The results in different steps of the analyses are summarized in Table 1.



1a 1b

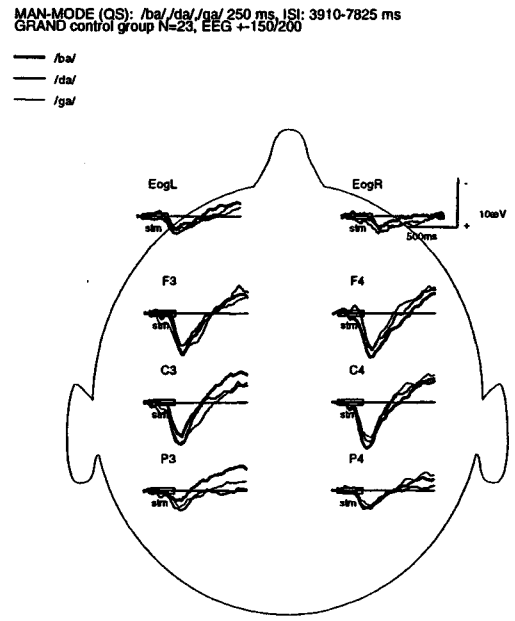
FIGURE 1. Principal components (PC1-4) in the synthetic stimuli set (1a), in and the natural stimuli set (1b). Control group included. Latency ranging from 0-950 ms.

In the next step, the factor scores of four factors in the synthetic stimulus set were selected for further MANOVA/ANOVA for repeated measures analyses. For Factor 1, there was Consonant (/ba/ or /da/ or /ga/) x Anterior-posterior distribution (frontal or central or parietal) interaction. A contrast indicated that responses for /ba/ at the frontal and central channels (F3, F4, C3, and C4) were different from those obtained for /da/ at the same channels, $F(1, 22) = 5.63$, $p < .027$. As can be seen in Supplement 1, the factor scores for response to /ba/ were more negative than those for /da/ in the central channels. An other contrast indicated that responses to /ba/ at the fronto-central (frontal and central channels were combined) and parietal (P3, and P4) channels differed from those elicited by /da/ at the same channels, $F(1, 22) = 8.16$, $p < .009$. The factor scores for /da/ in the parietal channels were more positive than those for /ba/ (see Supplement 1). For Factor 1, there was also a Consonant x Hemisphere interaction, and a contrast indicated that this interaction originated from the effect that /ga/ elicited a different response than /ba/ and /da/ between hemispheres, $F(1, 22) = 4.36$, $p < .049$. The factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, the scores for /ba/ and /da/ were more positive in the right hemisphere (see Supplement 1).

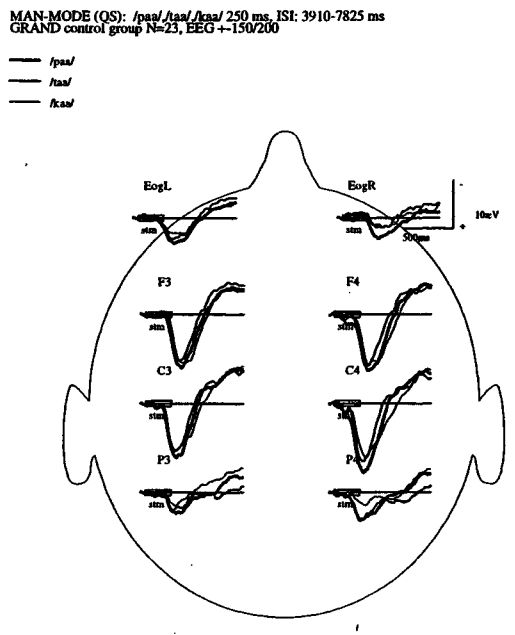
For Factor 2, there was a same kind of Consonant x Hemisphere interaction than for Factor 1, $F(2, 21) = 3.48$, $p < .050$, $\Lambda = .751$. A contrast indicated that responses to /ga/ differed from those to /ba/ and /da/ between hemispheres also in this factor, $F(1, 22) = 4.84$, $p < .039$. As can be seen in Supplement 2, the factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, scores for /ba/ and /da/ were more positive in the right hemisphere also in this factor. In addition, there was a main effect for Anterior-posterior distribution, $F(2, 21) = 7.81$, $p < .003$, $\Lambda = .573$. Contrasts indicated that the responses at the frontal channel differed from those at the central sites, $F(1, 22) = 11.20$, $p < .003$, and that the anterior electrode sites (frontal and central combined) differed from those at the parietal sites, $F(1, 22) = 14.66$, $p < .001$. For Factor 3, there was a Consonant x Anterior-posterior interaction, $F(4, 19) = 6.15$, $p < .002$, $\Lambda = .436$, and contrasts indicated that all of the consonants elicited a different frontal versus central responding in this factor (/ba/ from /da/, $F(1, 22) = 11.17$, $p < .003$; /ga/ from /ba/ and /da/, $F(1, 22) = 15.96$, $p < .001$). The scores for /ba/ in the central channels were the most positive ones, and the scores for /da/ in the frontal channels were the most negative ones (see Supplement 3). There were no statistically significant effects found for Factor 4. These results are summarized in Table 1.

The same analysis procedure was used for the four factor scores of the natural stimulus set (See Fig. 2b, and Table 1). For Factor 1, 2 , and 4 there was a main effect for Anterior-posterior distribution ($F(2, 21) = 6.57$, $p < .006$, $\Lambda = .651$ for Factor 1; $F(2, 21) = 19.63$, $p < .000$, $\Lambda = .348$ for Factor 2; and $F(2, 21) = 5.18$, $p < .015$, $\Lambda = .670$ for Factor 4, respectively). Contrasts indicated that there were differences across stimuli between the electrode channels. In Factor 2, there was also a main effect for the Consonant (/paa/ or /taa/ or /kaa/), and contrast indicated that in this factor the responses to /kaa/ differed from /paa/ and /taa/, $F(1, 22) = 4.76$, $p < .040$. In general, the factor scores for /kaa/ were more negative across channels. In Factor 3 there was a Consonant x Anterior-posterior distribution interaction, $F(4, 19) = 5.40$, $p < .004$, $\Lambda = .468$, and contrast indicated that the response between /kaa/ was differentiated from /paa/ and /taa/ also in this factor, $F(1, 22) = 11.37$, $p < .003$. As can be seen in

Supplement 4, the scores for /kaa/ in the parietal sites were more positive than those to /paa/ or /taa/.

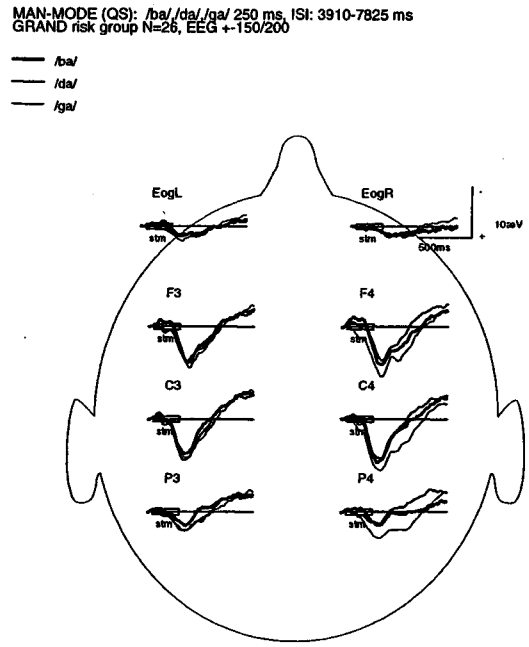


2a

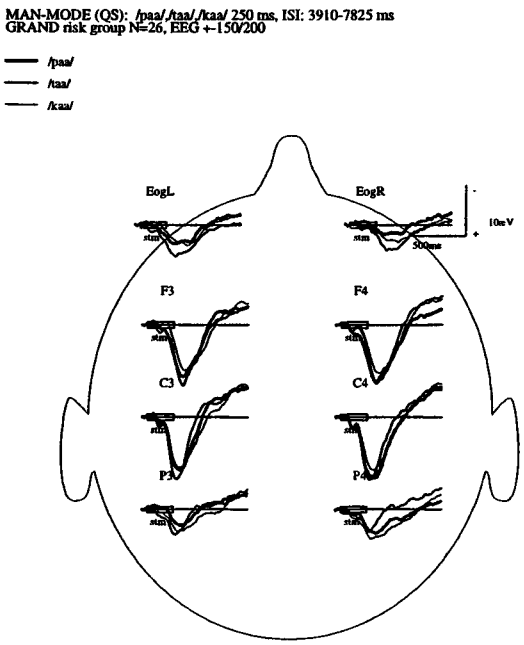


2b

FIGURE 2. The grand-averaged event-related potentials (ERPs) of the control group (n = 23) to a) synthetic (/ba/, da/, /ga/), and b) natural (/paa/, /taa/, /kaa/) CV-syllables. Time course is 950 ms with negativity up. The calibration marker is 10 μV.



3a



3b

FIGURE 3. The grand-averaged event-related potentials (ERPs) of the risk (n = 26) to a) the synthetic (/ba/, da/, /ga/), and b) natural (/paa/, /taa/, /kaa/) CV-syllables. Time course is 950 ms with negativity up. The calibration marker is 10 μV.

TABLE 1. PCA and MANOVA/ANOVA for repeated measures analyses for synthetic and natural CV-syllables. Control group (n = 23) included in the analyses.

	Synthetic stimuli			Natural stimuli		
	% of total variance	**Latency[a], ms (max loading, ms)**	**MANOVA effects (repeated measures)**	**% of total variance**	**Latency[a], ms (max loading, ms)**	**MANOVA effects (repeated measures)**
Factor 1	31.8 %	555-950 (825)	• Cons x Ant-post (ANOVA)*/** • Cons x Hem (ANOVA)*	30.0 %	555 -950 (875)	• Ant-post **
Factor 2	30.0 %	235-695 (485)	• Ant-post ** • Cons x Hem *	24.0 %	135 -515 (305)	• Cons (ANOVA) * • Ant-post ***
Factor 3	16.2 %	85-375 (215)	• Cons x Ant-post **	20.2 %	385-705 (535)	• Cons x Ant-post **
Factor 4	11.2 %	000-165 (45)	-	15.2 %	000-235 (65)	• Ant-post *
Total	89.1 %			89.5 %		

Note.[a]Factor loadings > .4. *$p \leq .05$. **$p < .01$. ***$p < .001$

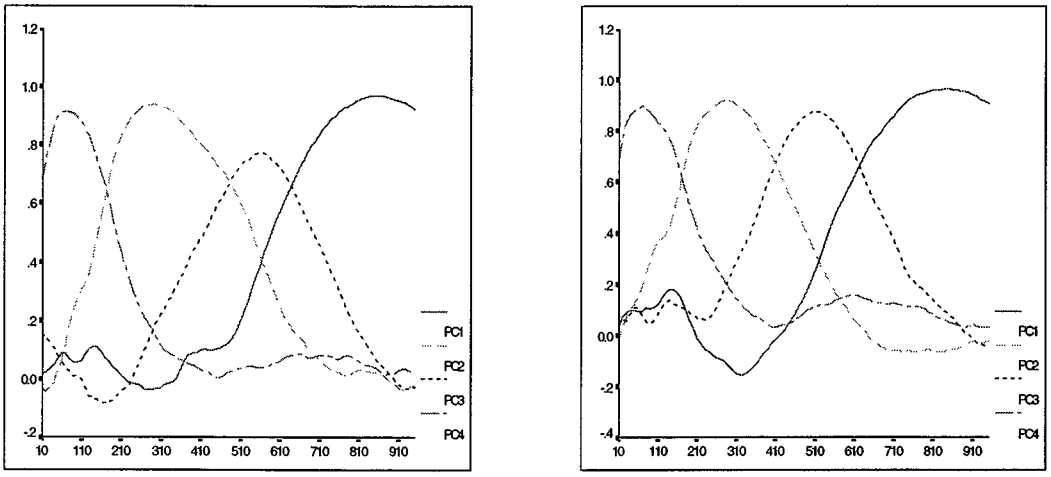
TABLE 2. PCA and MANOVA (and ANOVA) for repeated measures analyses for synthetic and natural CV-syllables. At-risk group (n = 26) and control group (n = 23) included in the analyses.

	Synthetic stimuli			**Natural stimuli**		
	% of total variance	**Latency[a], ms (max loading, ms)**	**MANOVA group-effects (rep. meas.)**	**% of total variance**	**Latency[a], ms (max loading, ms)**	**MANOVA group-effects (rep. meas.)**
Factor 1	30.2 %	565-950 (855)	• Cons x Ant-post x Group (ANOVA) *	31.2 %	535 -950 (835)	-
Factor 2	28.4 %	135-555 (285)	• Ant-post x Hem x Group*	22.4 %	135 -475 (275)	-
Factor 3	16.4 %	375-715 (565)	• Cons x Hem x Group*	20.6 %	345-695 (505)	• Cons x Ant-post x Group*
Factor 4	14.2 %	000-205 (65)	-	14.1 %	000-205 (65)	-
Total	89.3 %			88.6 %		

Note.[a]Factor loadings > .4. *$p < .05$.

3.2. Risk versus control group

Participants from the at-risk and the control group were included in the same analyses in order to determine Whether any differences could be found between the speech cue processing in these two groups. For the ERP data generated by the synthetic stimulus set, four principal components (PCs) or factors accounted for 89.3 percent of the total variance in the synthetic stimuli set. For the ERP data generated by the natural stimuli set there were four factors, respectively, which accounted for 88.6 percent of the total variance in the natural stimuli set. The factor loadings are presented in Fig. 4a (factors from the synthetic stimuli set), and in Fig. 4b (factors from the natural stimuli set). The results in different steps of the analyses are summarized in Table 2. When both groups were included in the same PCA in the natural stimuli set, the factor scores were approximately on the same latencies as those obtained from the PCA where only the control group was included (compare Figures 1b and 2b, and Tables 1 and 2). In the synthetic stimuli set, Factor 1 and Factor 4 were also approximately on the same latencies in these two different PCAs, but the latencies of Factors 2 and 3 were reversed (compare Figures 1a and 4a, and Tables 1 and 2).



4a 4b

FIGURE 4. Principal components (PC1-4) in the synthetic set (4a), and in the natural stimuli set (4b). Both groups included. Latency ranging from 0-950 ms.

In the synthetic stimuli, a significant Consonant response (/ba/ or /da/ or /ga/) x Anterior-posterior distribution x Group interaction (risk or control) was found for Factor 1. As indicated by the difference contrast, this interaction was based on the fact that /da/ evoked a different parietal response than /ba/ in the control and in the at-risk group, $F(1, 47) = 8.05$, $p < .007$. As can be seen in Supplement 5, in the control group the factor scores for response to /da/ were more positive than those for /ba/ in the parietal channels. This pattern was reversed in the at-risk group: the factor scores to /da/ were more negative than those for /ba/. A significant Anterior-posterior distribution x Hemisphere x Group interaction was found for Factor 2, $F(2, 46) = 3.23$, $p < .049$, $\Lambda = .877$. When tested with contrast, this effect reflected differences in responding in the parietal sites between groups, $F(1, 47) = 6.60$, $p < .013$. In the control group, the factor scores for the parietal responses were more negative in the left hemisphere, but on the contrary, this pattern was in the right-hemisphere in the at-risk group (see Supplement 6). A Consonant response x Hemisphere x Group interaction was observed for Factor 3, $F(2, 46) = 3.80$, $p < .030$, $\Lambda = .858$, and as indicated by contrast, this originated from the effect that that /ga/ elicited a different hemispheric response between groups, $F(1, 47) = 7.37$, $p < .009$. As can be seen in Supplement 7, in the control group the factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, in the at-risk group the similar pattern was in the right hemisphere. These results are summarized in Table 2.

In the natural stimulus set, only for Factor 3 revealed a significant group interaction, namely a Consonant (/paa/ or /taa or /kaa/) x Anterior-posterior x Group interaction, $F(4, 44) = 3.27$, $p < .020$, $\Lambda = .771$. As indicated by a contrast, this interaction originated from the effect that /kaa/ elicited a different parietal response between groups, $F(1, 47) = 9.11$, $p < .004$. As can be seen on Supplement 8, when compared to the control group, the at-risk groups' factor scores for /kaa/ in the parietal sites were similar to those for central channels.

Discriminant function analysis was used to test how well group membership (at-risk vs. control) could be determined by the factor scores that contributed to group interactions in both synthetic and natural stimuli sets. In the synthetic stimuli set there were following factor score combinations: For Factor 3, the scores for /ba/ + /da/ in

the left hemisphere (LBADA), and /ba/ + /da/ in the right hemisphere (RBADA) were combined. The factor scores to /ga/ (which elicited different responses than two other stimuli) were summed across left and right hemisphere similarly. Resulting composite scores were /ga/ in the left hemisphere (LGA) and /ga/ in the right hemisphere (RGA). For Factor 1, the composite scores were /ba/ and /da/ calculated from frontal and central channels (BAFC, DAFC) and parietal channels (BAP, DAP). For Factor 2 the composite scores were calculated by summing the responses from the frontal and central versus the parietal channels in both hemispheres (LFC, RFC; LP, RP). In natural stimuli set, the new variables for Factor 3 were calculated by adding responses to /paa/ and /taa/ from the frontal and central sites versus the parietal sites (PAATAAFC, PAATAAP), and a composite scores for responses to /kaa/ (which differed from the other two stimuli) were calculated similarly (KAAFC, KAAP). Altogether, there were 16 composite scores which differentiated the groups with the accuracy of 91.84 %, $\chi(16, n = 49) = 36.2$, $p < .003$, $\Lambda = .395$; 92.3 % of the cases were correctly classified as belonging to the at-risk group (24 from 26), and 91.3 % to the control group (21 from 23).

4. DISCUSSION

At the first step in our study, we studied only the participants from control group in order to get a normative picture about the speech cue processing of the newborns. In general, there were noteworthy similarities between the newborn ERPs elicited by synthetic stimuli (/ba/, /da /ga/) in our study and responses to /ba/ and /da/ in the studies of Kurtzberg, Stone, and Vaughan (1986), and Kurtzberg, Vaughan, and Novak (1986): in these studies the ERP responses were characterized by an initial positive peak at 110 ms, largest positivity around 300 ms, and later occurring negativity (in the study of Kurtzberg et al. this later negativity peaked around 600 ms, and in our study it was around 800-950 ms). These similarities indicate that the ERP methodology is a reliable tool for the measurement of speech cue processing in newborn infants.

Starting from the beginning of the time window, there were no significant effects in Factor 4 (from the stimulus presentation to 165 ms, peak at 45 ms) in the synthetic stimuli set (/ba/, /da/, and /ga/). In other words, there were no differences in the cortical activation evoked by different stimuli at this early stage of processing. This is something which one should expect, because this early factor reflects obligatory responses; in other words, the overall responsiveness of the brain to stimuli (Friedman, 1990, Leppänen et al., 1997). The differentiation between the stimuli occurred in a later stage of the processing, which was reflected by Factors 3, 2, and 1. Around 215 ms (Factor 3), both hemispheres differentiated consonants in a similar manner; in other words there were divergences in anterior-posterior distribution elicited by different consonants only within hemispheres. However, there was an interesting change in this pattern in later phase. It appeared that from the latency of 240 ms onward the role of the left hemisphere was emphasized. Around 485 ms (Factor 2) the hemispheres diverged from each other according to their responses to different consonants; factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, scores for /ba/ and /da/ were more positive in the right hemisphere. And finally, in the latest stage (around 825 ms, Factor 1) there was the

same kind of differential response than in Factor 2; namely the left hemisphere differentiated /ga/ from /ba/ and /da/ in this time window also. In this latest time window there were also bilateral consonant differentiation effects (the factor scores for /da/ in the parietal channels were more positive than those for /ba/). For Factor 1, there was high loading towards the end of the analyzed time window (the same was found also in the natural stimuli set, and in the analysis where both groups were involved). According to Wastell (1981b), this kind of trend is obtained when the used baseline has a wide window (for example, up to 1 sec) before the stimulus presentation, and this component usually does not show any meaningful statistical effects. But as van Boxtel (1998) suggested, this effect is minimized if the baseline is situated at the beginning of the analyzed time window, as was the case in our study.

These results obtained from the control group are consistent with the evidence that that speech and language functions are primarily lateralized in the left hemisphere even in this early state of development (Bryden, 1982; Hiscock, 1988; Segalowitz, 1983; Witelson, 1987). Our results also partially replicated the studies of Molfese and Molfese (1979a, 1985, 1997) and Molfese et al. (1991). Factor 2 (between 235-695 ms, peak at 485 ms) showed similar patterns as the factors in the studies of Molfese et al., (Molfese and Molfese 1979a: Factor 4 between 128-272 ms; Molfese and Molfese, 1985: Factor 3 between 88-240 ms; Molfese et al. 1991: Factor 3 between 80-330 ms; Molfese and Molfese, 1997: Factors 2 and 6 between 70-320 ms), namely the ability of the left hemisphere to discriminate between different consonants. In the studies of Molfese and Molfese, and Molfese et al. this differentiation was between /b/ and /g/ contrasts, as was the case in our study also. In our study (and also in the study of Molfese and Molfese, 1997) the consonant-vowel syllable /da/ was included in the stimuli set, but the clearest differences in the responses were evoked by /ga/ compared to the two other stimuli.

The late Factor 1 (555-950 ms, peak at 825 ms) also reflected the ability of the left hemisphere to differentiate between /ga/ from /ba/ and /da/. In addition, this component also reflected a bilateral differentiation, namely between /ba/ and /da/. In the studies of Molfese and Molfese, and Molfese et al. there was also the same kind of late bilateral consonant differentiation, with the exception that the differentiation was

between /b/ and /g/ (Molfese and Molfese 1979a: Factor 3 between 490-704 ms; Molfese and Molfese, 1985: Factor 7 around 664 ms; Molfese et al. 1991: Factor 3 between 520-700 ms).

Despite these similarities, there were also certain differences between our results and those obtained by Molfese et al. Namely the components which could differentiate /b/ and /g/ contrasts appeared at an earlier latency in the studies of Molfese et al (70-330 ms) than in our study (235-695 ms). These differences could be partially explained by the differences between the experimental variables (Gelfer, 1987), such as speech versus nonspeech formant structure (Molfese and Molfese, 1979, 1980, 1985; Molfese et al., 1991), or phonetic versus nonphonetic transition structure (Molfese and Molfese, 1980), which were not included in our study. Another important difference is the arousal state of the participants. In the studies of Molfese et al. (Molfese and Molfese, 1979, 1980), as well as in our study, the participants were in the quiet sleep state, whereas in the other studies (Molfese and Molfese, 1985, 1997; Molfese et al., 1991) the stimuli were only presented when infants were in the quiet awake state. As shown, for example, by Scucard et al. (1987), in particularly the later ERP peaks in wakefulness state differed from the responses of sleeping infants.

The more specific differences between our study and those of Molfese et al. are the electrode channels used in these studies. Molfese et al. used different electrode channels in different stages of their research history. In the earlier studies (Molfese and Molfese, 1979, 1980, 1985), only T3 and T4 channels were used, and later on electrodes over frontal and parietal scalp areas were also utilized (Molfese, 1989; Molfese and Molfese, 1997; Molfese et al., 1991). In our study, the frontal, central and parietal channels were used. There was also differences between analysis methods, namely in the association matrix selection for the principal component analysis (PCA). Molfese et al. extracted components from the covariance matrix, but in our study we used the correlation matrix for this purpose. The standardization of the ERP data was also done differently, namely in the studies of Molfese et al. the data were normalized before entering to PCA, and in our study, they were normalized by PCA.

One important difference between our study and those of Molfese et al. was the inclusion of the natural stimuli (/paa/, /taa/, and /kaa/). There were interesting differences in the component structure elicited by the synthetic and natural stimuli. In early latency (Factor 4), there was an effect which was not found in the synthetic set. This was characterized by the difference of the overall responding of the frontal and central electrode locations, but which was not yet effected by consonant differences (obligatory responding). The most interesting aspects were those concerning these consonant differentiation effects, which were found only for Factor 2 (135 - 515 ms, peak at 305 ms) and Factor 3 (385 - 705 ms, peak at 535 ms), but not in the latest time window (Factor 1, 555-950 ms , peak at 875 ms). These effects were composed differentially than in synthetic sounds. At first (Factor 2) /kaa/ was differentiated from /paa/ and /taa/ without any correspondence to the brain locations (Consonant main effect), but in the following time window (Factor 3) this same kind of differentiation was clearest in the parietal channels. In other words, there were no hemispheric effects related to consonant differentiation in the natural stimuli set. From these differences between the stimuli sets, it could be concluded that natural and synthetic stimuli elicit different kinds of responses in newborns (see also Gelfer, 1987).

The conclusion that these differences were mainly affected by the origin of the two sets (synthetic versus natural) rather than by their differences in voice onset times (in other words, are sounds heard as /b/ or /p/, /d/ or /t/, and /g/ or /k/), was based on the fact that there were clearer differences between rather than within the stimulus sets. The amplitude elicited by the natural stimuli was increased (compare Figures 2a versus 2b, and 3a versus 3b), which also could be seen in the single subject level. This trend could be explained by the fact that natural sounds have richer auditory features. Synthetic stimuli varied only according to their transitions (Stevens and Blumstein, 1978), but in the natural set this variation was much broader. The natural stimuli varied also according to other speech cues such as bursts of acoustic energy occurring at consonantal release (Stevens and Blumstein, 1978). We can speculate that this is how natural sounds also activated broader neuronal networks, which were manifested in increased amplitudes seen in the responses.

The main interest in this study were the possible differences in ERP responses to various consonants between the at-risk and the control groups: in other words, whether the speech sound processing of newborns with the genetic risk for later language problems is different from that of newborns without such a risk. There were clear results that indicated that cortical activation evoked by speech elements (rapid transitions differentiating between various consonants) is different in infants at-risk for dyslexia already at this early stage of development. In the synthetic stimuli set, there were not any significant effects in early latency (Factor 4, from the beginning of the stimulus presentation to 205 ms, a peak at 65 ms), as was the case in the control group only-analysis. The earliest significant group related differences was found for Factor 2 (between 135 - 555 ms, a peak at 285 ms). In the control group the factor scores for the parietal responses were more negative in the left hemisphere, but on the contrary, this pattern was in the right hemisphere in the at-risk group. However, the effects relating to consonant differentiation were found in the later latency. For Factor 3 (between 375 -715 ms, peak at 565 ms), these effects appeared in the most interesting manner: in the control group the factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, in the at-risk group the similar pattern was in the right hemisphere. This kind of different hemispheric responding can also be seen in the original ERP averages (compare Figures 2a and 3a). In the last phase (Factor 1, peak at 855 ms), control groups' factor scores for /da/ were more positive than those to /ba/ in the parietal channels. This pattern was reversed in the at-risk group (the factor scores for /da/ were more negative than those for /ba/).

Interestingly, the differences between the groups were not so clear in the natural stimuli set. Only for Factor 3 (345-695 ms, peak at 505 ms) were there group related effects: when compared to the control group, the at-risk groups' factor scores for /kaa/ in the parietal sites did not differ from those for central channels. There were no hemisphere-related effects in the group comparisons. These differences in discriminative features in the synthetic and natural stimuli sets could be explained, as noted earlier, by the fact that natural stimuli are richer in their auditory features, and therefore easier to differentiate from each other. In other words, these differences could be easier to differentiate not only for the control group, but also for the risk

group. This is one possible explanation as to why such clear group related effects were not found in the natural stimuli set.

Both in the synthetic and natural stimuli sets (and also in the control group only -analysis, and in the both groups included -analysis) there was an interesting trend in consonant differentiation. The responses for /ba/ and /da/ were similar in the sense that there were no statistically significant differences between them, except between /ba/ and /da/ in the latest latency (Factor 1). However, responding to /ga/ was different from the two former syllables, and this differentiation elicited the clearest hemispheric differences both in the control group only and in the between groups-situations. This trend was also found in the natural stimuli set: namely /kaa/ elicited the clearest differences compared to /paa/ and /taa/. These results can be explained in view of the differences in place of articulation; in other words, differences in the production source of a vocal-tract (Blumstein and Stevens, 1979). The stimuli which were produced in the palatal-velar/back positions (/k/, /g/) were more clearly differentiated from the stimuli produced in the labial/frontal (/p/, /b/) and alveolar/middle (/t/, /d/) positions (Borden and Harris, 1981). However, from the standpoint of the receptive processing capacities of the brain, the more interesting explanation comes from the differences of the transition continuum between the stimuli: /ga/, which can be located at the falling transition end of the continuum, elicited more different responding than /ba/, which was characterized by sharply rising transitions, and /da/, which was characterized by the less sharp or falling transitions (Borden and Harris, 1981).

The results obtained from our study have some interesting similarities with dyslexia studies with older participants. The most interesting connection could be drawn from the results concerning the clear hemispheric differences in speech cue processing based on Factor 3 in the synthetic stimuli set (in the control group the factor scores for /ga/ were more positive in the left hemisphere, but on the contrary, in the at-risk group the similar pattern was in the right hemisphere). The control participants in our study differentiated these speech cues in the left hemisphere, which was line with the results of the newborn ERP studies of Molfese and Molfese (1979a, 1985, 1997) and Molfese et al. (1991), and with the behavioral evidence from older infants (Segalowitz, 1983; Witelson, 1987). The same kind of hemispheric differences between at-risk and

control groups have been found also in the other subsample of newborns which participated in the JLD-project (Leppänen et al., 1999, in press): significant stimulus (differing in vowel duration) and stimulus rate (slow rate condition, see also Pihko et al., 1999, in press) effects occurred more consistently in the left hemisphere in the control group while in the at-risk group it the right hemisphere. These results with two separate subgroups provide strong evidence that newborns with a genetic risk for dyslexia process auditory stimuli differently from infants without such a risk even from birth. The different ERP lateralization pattern of the at-risk group in this study and in the study of Leppänen et al. (1999, in press) could reflect the same kinds of deviations from the normal hemispheric lateralization found in behavioral (Bryden, 1988; Obrzut, 1988) and in anatomical and functional studies of older dyslexics. Results from anatomical and functional studies have concerned, for example, atypical patterns of cerebral lateralization (Dalby et al., 1998; Hynd and Semrud-Clikeman, 1989; Jernigan et al., 1991; Leonard et al., 1993), abnormal patterns of activation in left temporoparietal regions during phonological processing (Paulesu et al., 1996; Rumsey et al., 1992), and deviations from the usual pattern of left greater than right planum asymmetry (Galaburda et al., 1985; 1987; Humphreys et al., 1990; Hynd et al., 1990; Larsen et al., 1990; Rosen et al. 1993) among dyslexics. There is speculation that these latter findings of altered planum temporale asymmetry might explain the association with qualitative alterations in the functional properties of the system which can be seen, for example, in phonological coding deficits among dyslexics (Galaburda et al., 1987; Pennington, 1991).

There are also interesting relations between the results from our study and the role of developmental factors in the explanation of the abnormal anatomical findings among dyslexics: for example, as stated by Galaburda et al. (1994), symmetry of the medial genigulate nuclei (MGN) of the thalamus which handles rapid temporal transitions could result from abnormal development of this auditory subsystem. Furthermore, the cortical abnormalities (Galaburda et al. 1985; Humphreys et al., 1990; Rosen et al., 1993) found in dyslexics could originate prenatally during the period of neuronal migration and subsequent cortical maturation (Rosen, Press, Sherman, & Galaburda, 1992). These suggestions are in line with the results from our studies and the study of

Leppänen et al. (1999, in press): there were already differences in the cortical responding of the at-risk and the control groups at this newborn stage.

The fact that these differences between groups in speech cue processing could be obtained more clearly by using stimuli from the synthetic set than from the natural set could be explained, as noted earlier, by the fact that synthetic stimuli were harder to differentiate from each other than natural stimuli (synthetic stimuli varied only according to their brief formant transitions, but in the natural stimuli set this variation was broader). These results are in line with the evidence that older dyslexics have problems in differentiations about complex and rapidly changing acoustic temporal and spectral characteristics of a speech signal in a brief time window (Fitch et al., 1997; Tallal, 1980, 1984). Also the results from the ERP study (Leppänen et al., submitted) and a behavioral study (Richardson, 1998) with six-month-olds who participated in the JLD-project were in line with this suggested timing deficit. It should be noted, however, that with the procedure used in this study we cannot with any degree of certainty conclude that the differences in speech cue processing of the at-risk group would be purely a manifestation of underlying temporal processing deficit.

It could be summarized that in our study the speech cue processing of newborns with genetic risk for dyslexia was different from the matched control group. These results are consistent with the hypothesis that dyslexia is a genetically transmitted disorder. The same kind of evidence has also emerged from a prospective longitudinal study with older dyslexic children (Scarborough, 1990). Furthermore, these results are in line with the hypothesis of genetic influence-brain function-linkage in dyslexia. As noted earlier, we used newborns as participants in order to trace possible hereditary differences between infants at risk for later language deficit and those without such risk (minimizing the effect of environmental factors). On the basis of these results we could speculate that genetic factors contributed to the differences found in speech cue processing which, on the other hand, could be a manifestation of the influence of genetic factors on brain development (Pennington, 1991). Functional differences (especially hemispheric differences) between groups in speech cue processing could reflect the same kind of hemispheric deviations found in anatomical and functional

studies of older dyslexics. These deviations could, on the other hand, originate prenatally during the period of neuronal migration and subsequent cortical maturation (Rosen et al., 1992).

The functional influence of these differences of speech cue processing for later language development is a second important question. These differences between groups can also be explained by taking the view that newborn ERPs have successfully been used to predict later language development (Molfese and Molfese, 1985, 1997; Molfese and Searock, 1986). Molfese et al. suggested that the results of their studies could reflect a more sensitive nervous system of the high performance group. This more sensitive mechanism could make finer differentiations between a variety of auditory events that share some commonality with speech perception events, and the accuracy of this perceptual mechanisms creates a base for later language and cognitive processes. In other words, in a developmental context the deficits in auditory temporal processing could lead to impaired phonological perception and language development (Fitch et al., 1997). It should be noted, however, that in our study the differences in speech cue processing between groups were not so clear when the stimuli had richer discriminative features: natural stimuli were easier to differentiate not only for the control group, but also for the at-risk group. Considering these facts, we could speculate that the differences between groups should not be so extensive in a natural language environment where the richness of the auditory features could compensate for the deficits in auditory processing accuracy.

To summarize, even if this study provided some evidence for genetic influences-brain function differences-linkage in dyslexia, we cannot predict at this early state of our longitudinal study how these differences in speech cue processing will affect and appear in the future language development of our participants (behavioral manifestations of dyslexia). It remains to be seen in our further studies how these early differences between the at-risk and control group are related to possible later developing dyslexia.

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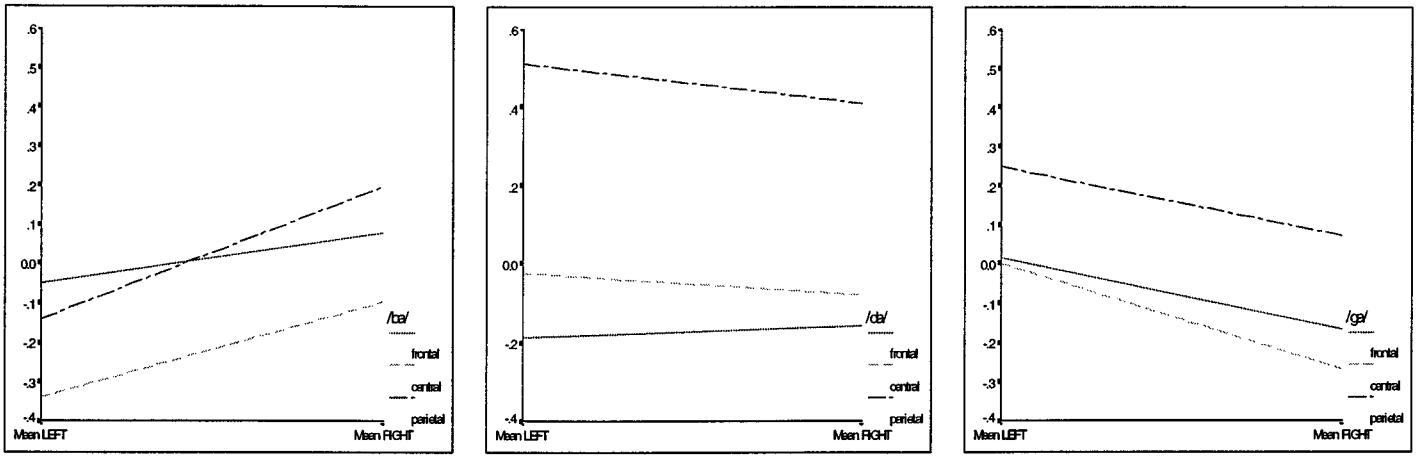
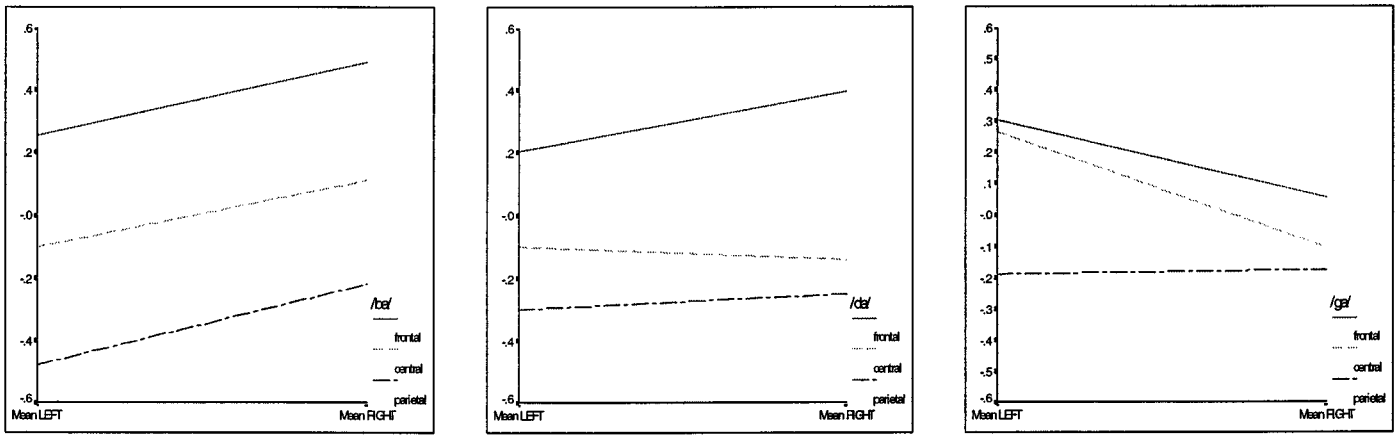
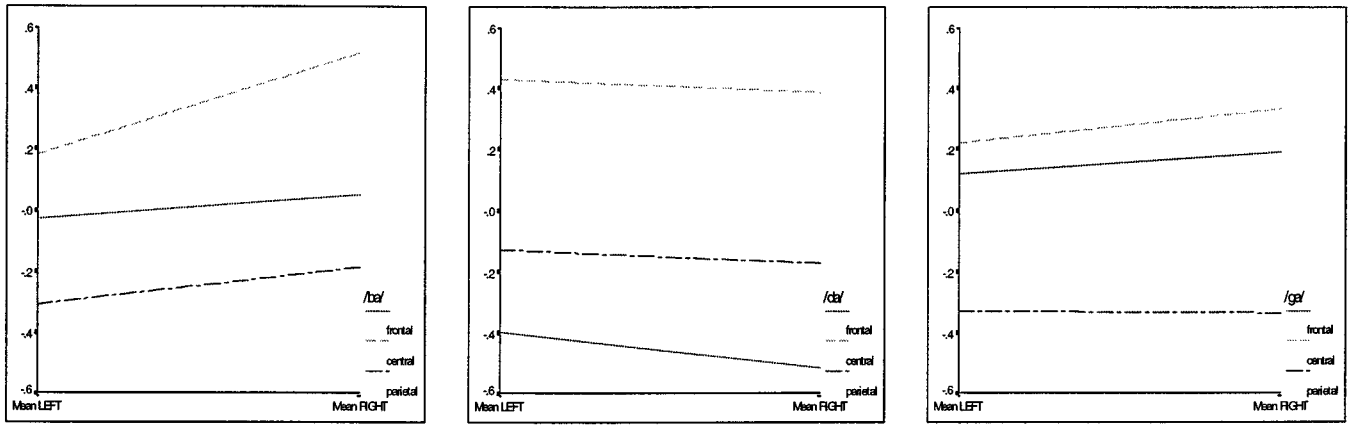
SUPPLEMENTS:



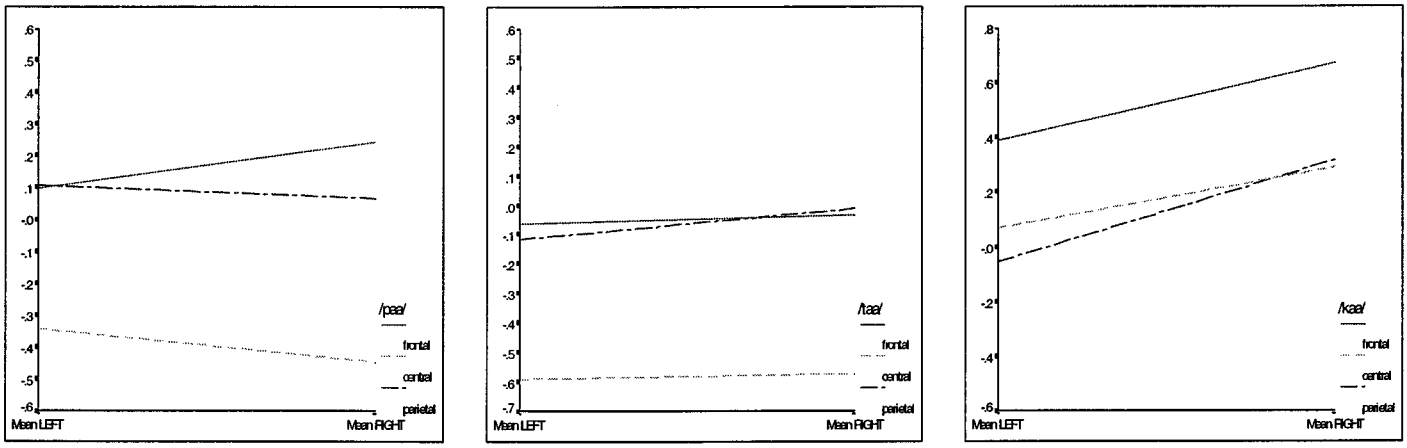
SUPPLEMENT 1. Factor 1 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23) to /ba/ (left graph), to /da/ (middle), and c) /ga/ (right). Factor scores for the frontal, central, and parietal channels included.



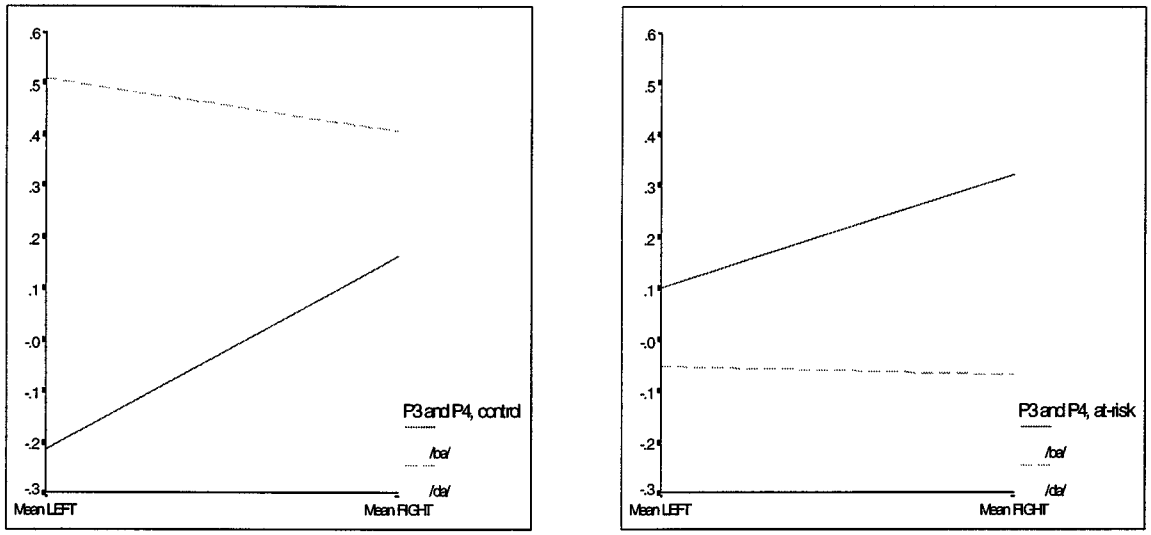
SUPPLEMENT 2. Factor 2 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23) to /ba/ (left graph), to /da/ (middle), and c) /ga/ (right). Factor scores for the frontal, central, and parietal channels included.



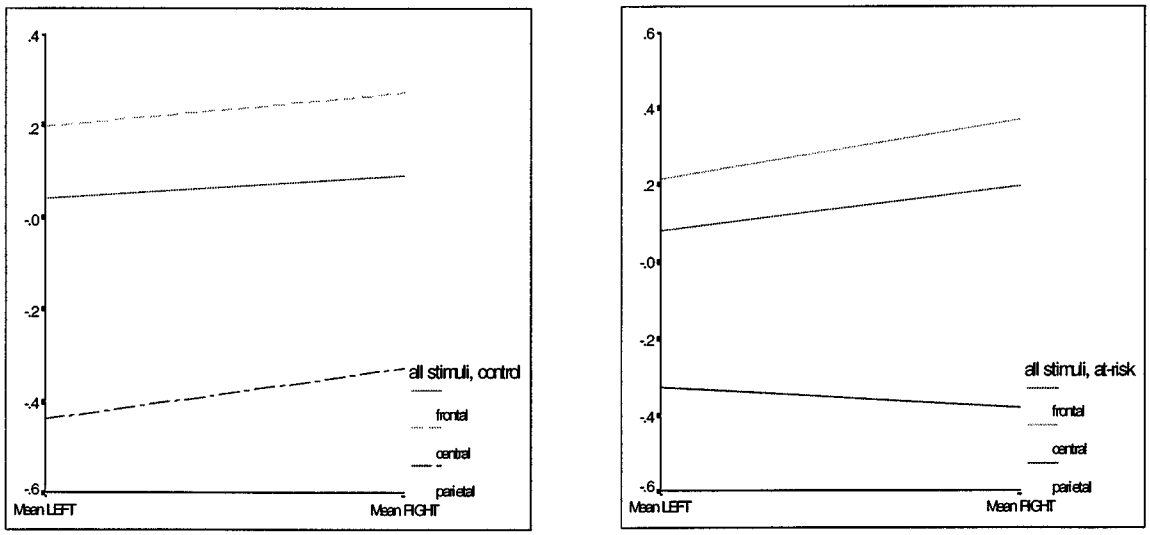
SUPPLEMENT 3. Factor 3 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23) to /ba/ (left graph), to /da/ (middle), and c) /ga/ (right). Factor scores for the frontal, central, and parietal channels included.



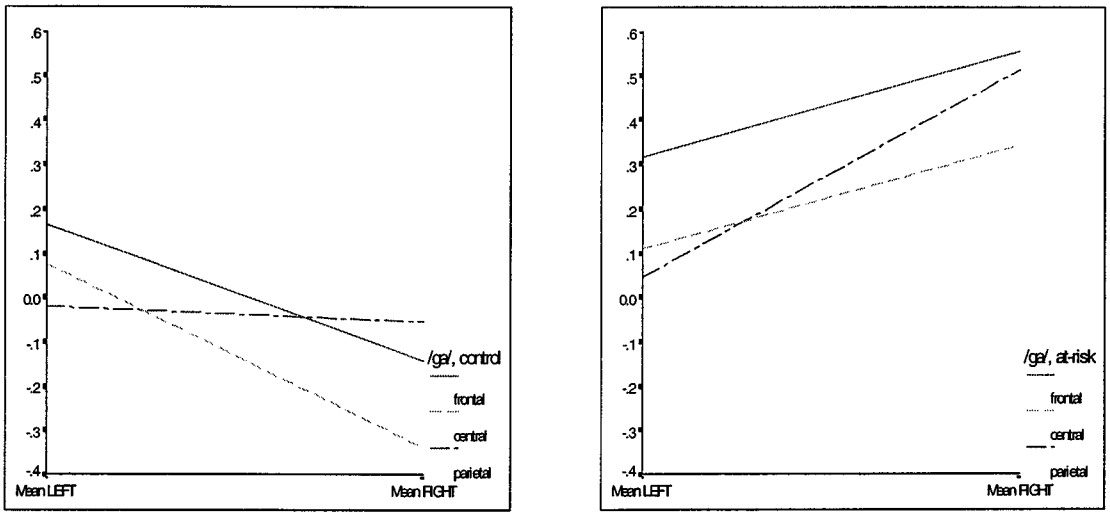
SUPPLEMENT 4. Factor 3 in the natural stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23) to /paa/ (left graph), to /taa/ (middle), and c) /kaa/ (right). Factor scores for the frontal, central, and parietal channels included.



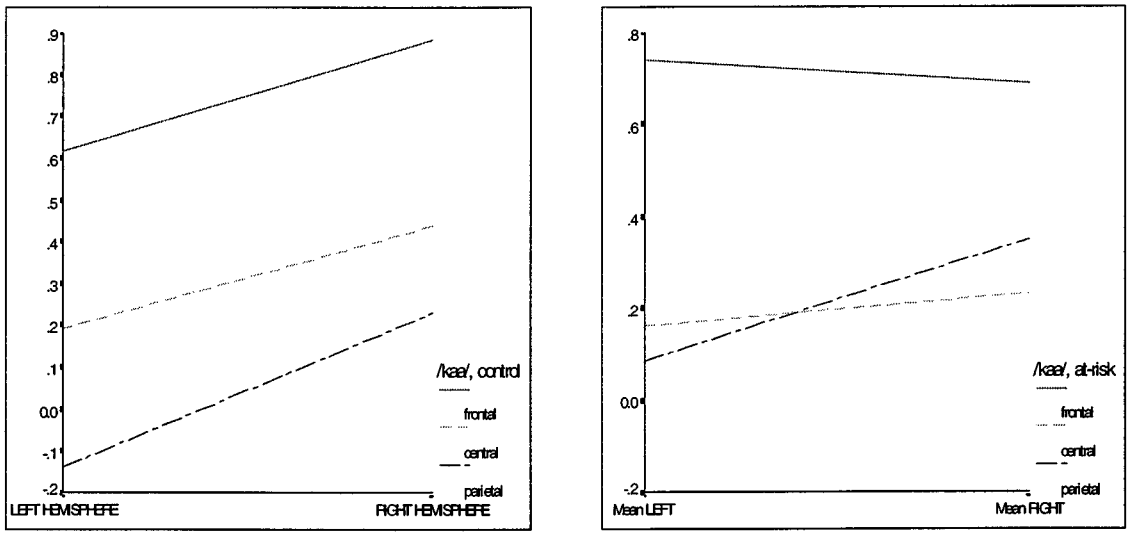
SUPPLEMENT 5. Factor 1 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23, in the left graph), and the at-risk group (n = 26, in the right graph). Factor scores for /ba/ and /da/ in the parietal channels included.



SUPPLEMENT 6. Factor 2 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23, left graph), and of the at-risk group (n = 26, right graph). Factor scores across stimuli in the frontal, central, and parietal channels included.



SUPPLEMENT 7. Factor 3 in the synthetic stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23, left graph), and of the at-risk group (n = 26, right graph). Factor scores for /ga/ in the frontal, central, and parietal channels.



SUPPLEMENT 8. Factor 3 in the natural stimuli: mean factor scores from the left and right hemisphere of the control group (n = 23, left graph), and of the at-risk group (n = 26, right graph). Factor scores for /kaa/ in the frontal, central, and parietal channels.