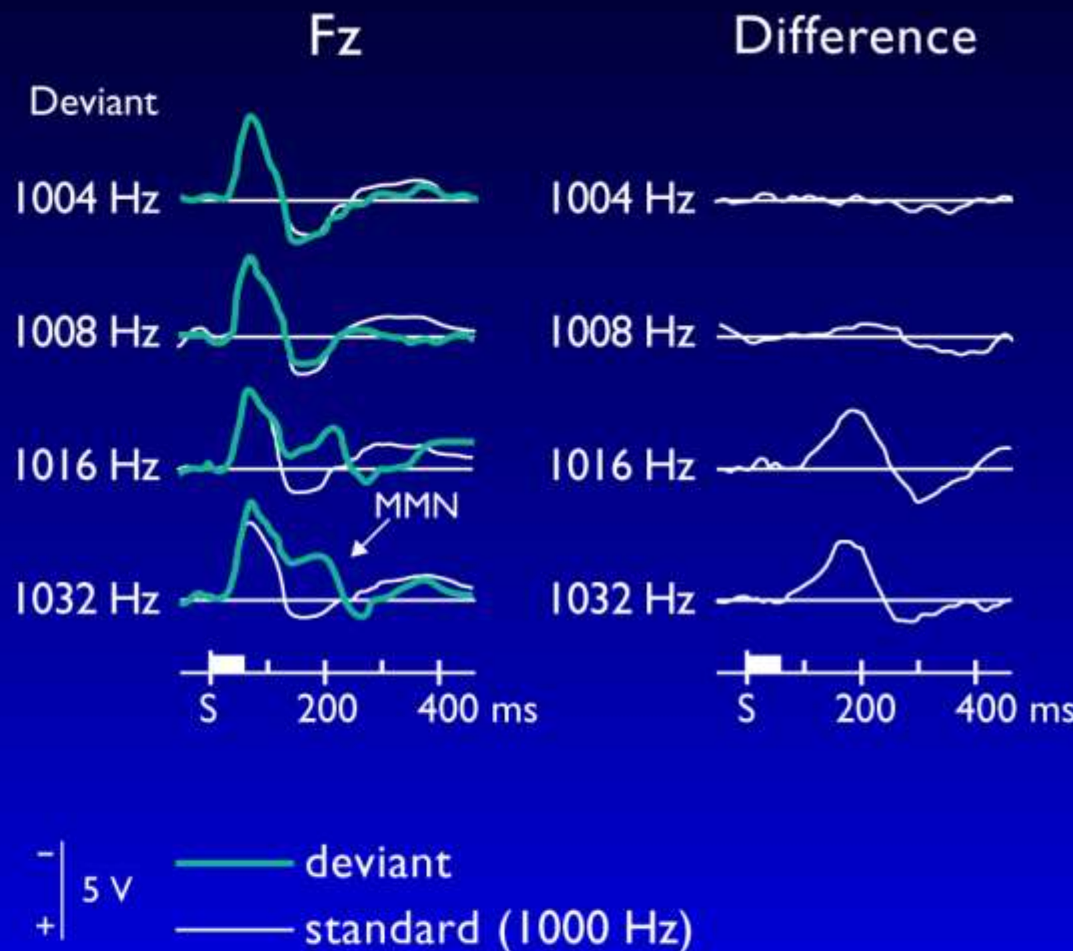
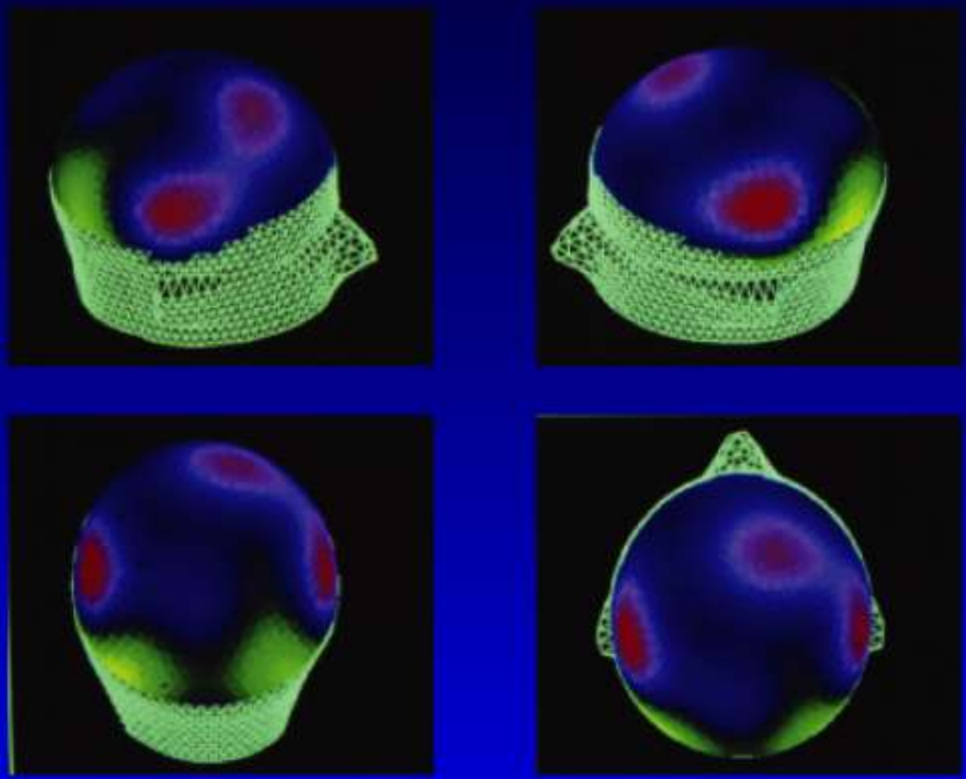
MMN as a Function of Frequency Change



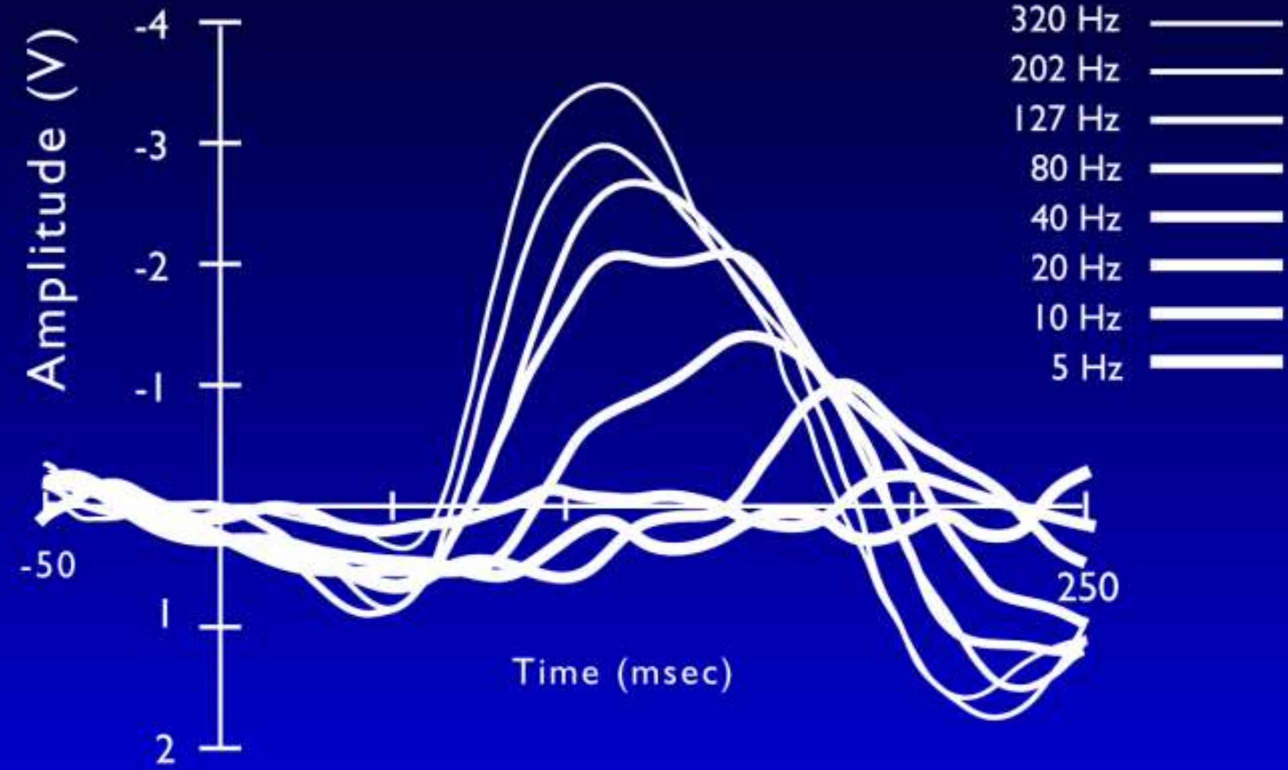
Sams *et al.*, 1985

Frequency MMN generators reflected by scalp current density analysis



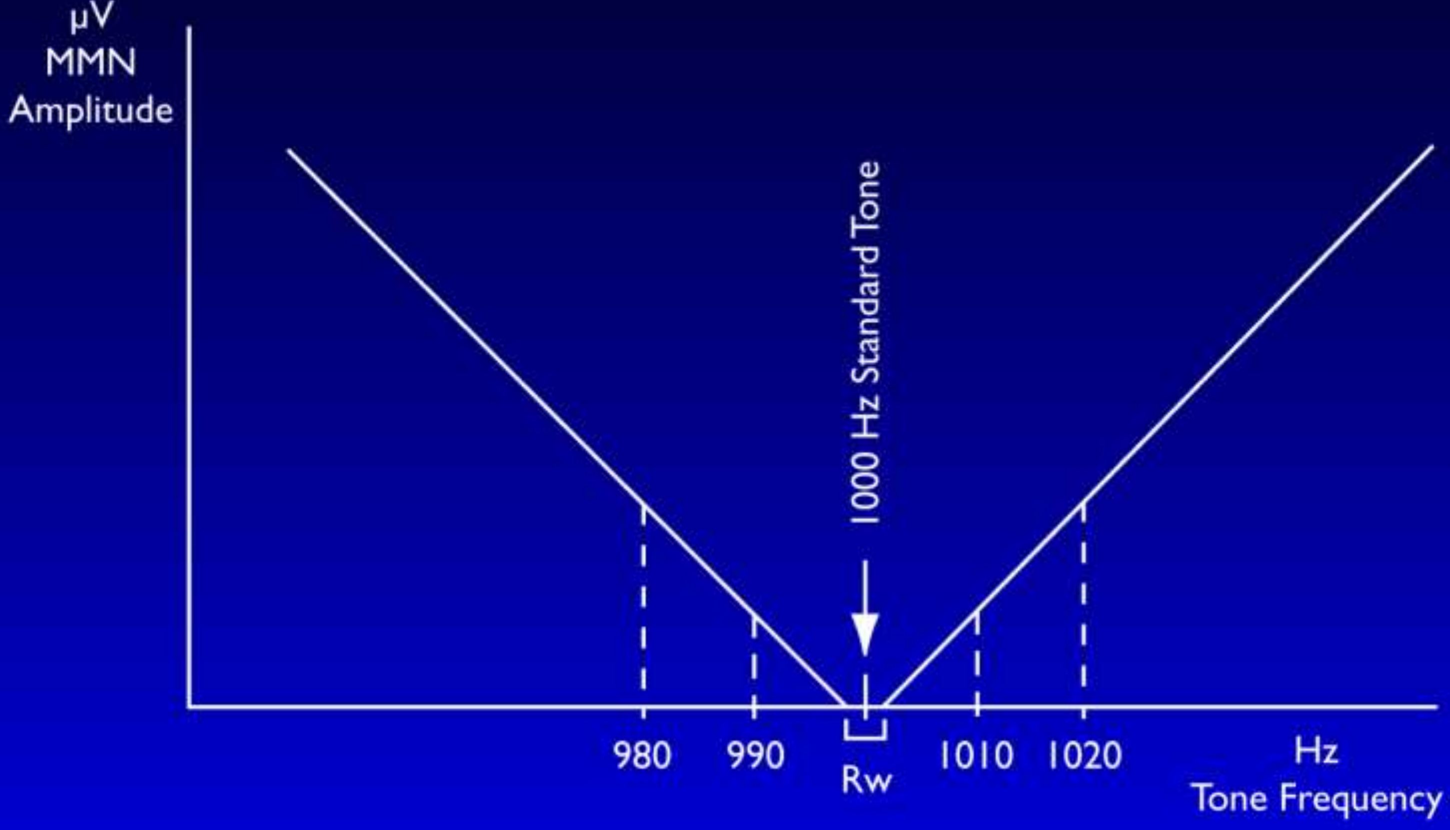
Compliment of Giard *et al.*, 1990

MMN as a Function of Deviance Magnitude



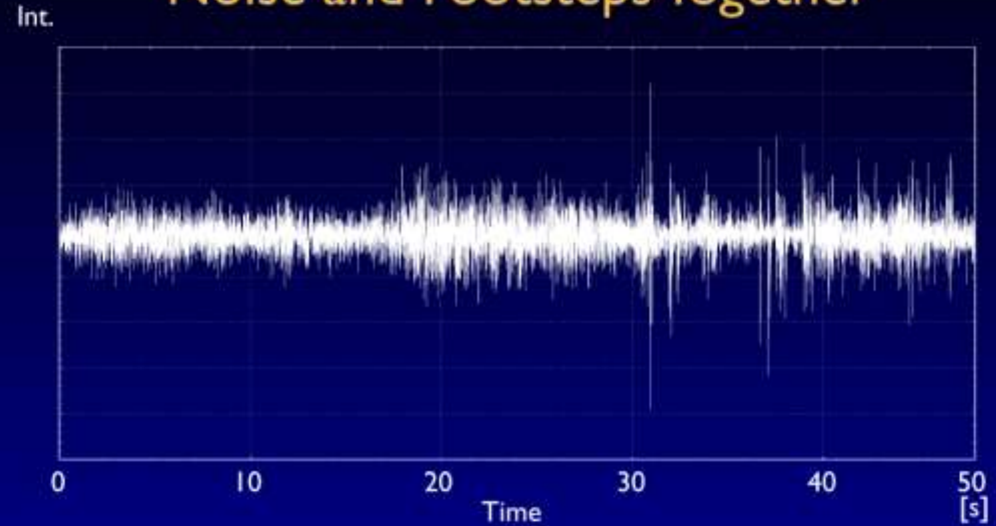
Tiitinen *et al.*, Nature 1994

MMN as a Function of Frequency Change

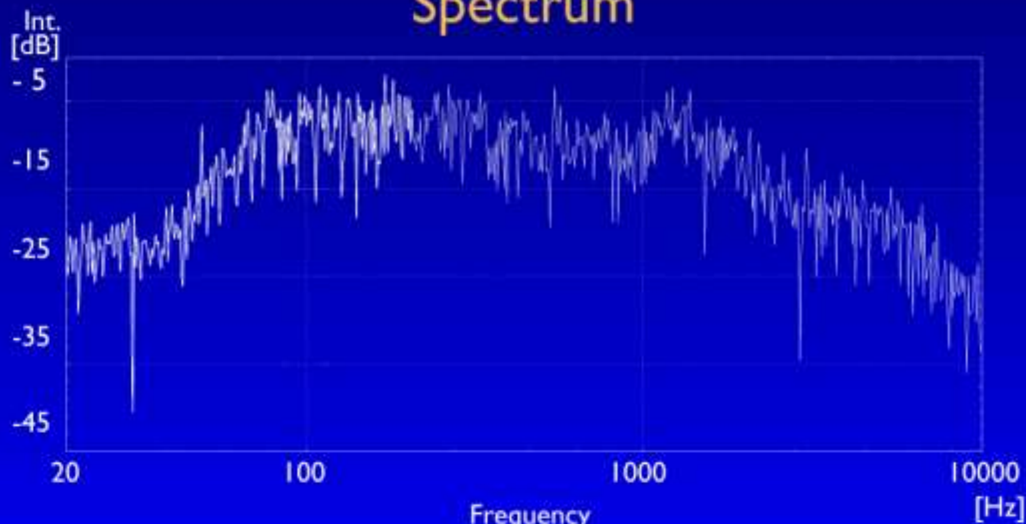


Näätänen & Alho, 1997

Noise and Footsteps Together

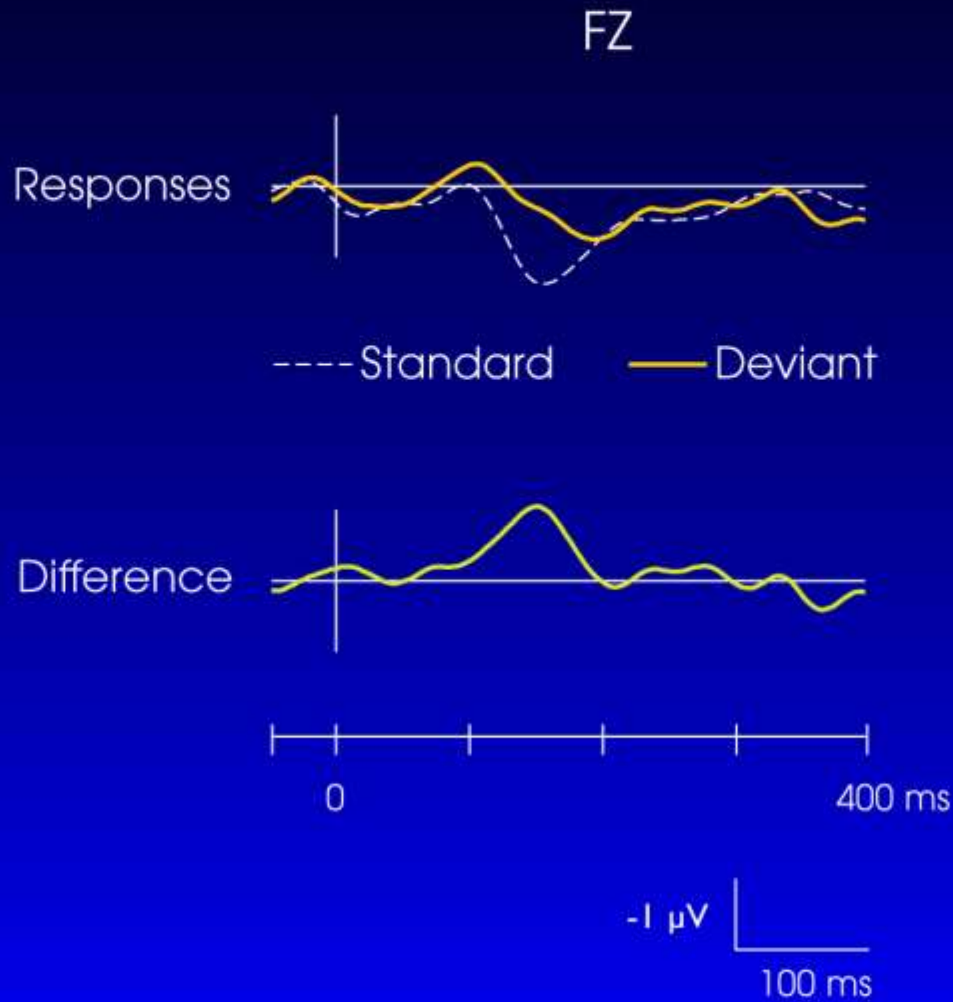


Spectrum



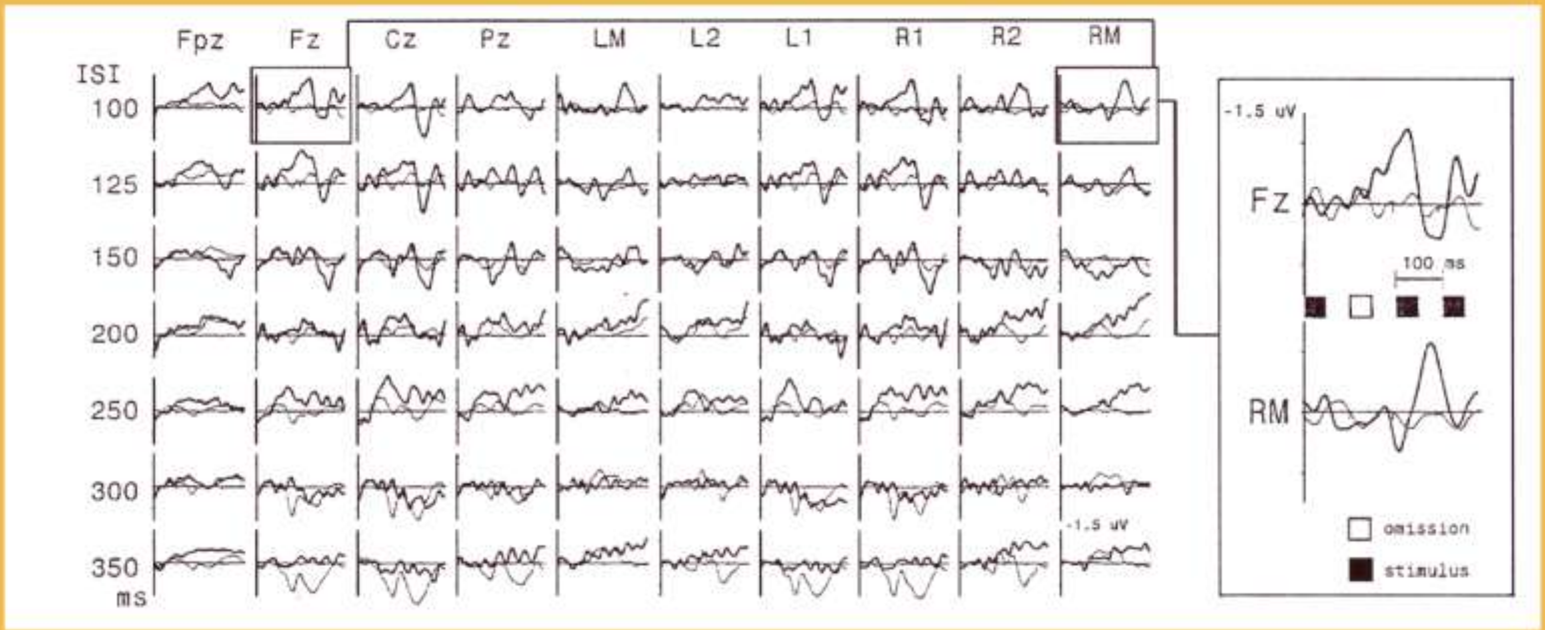
Winkler *et al.*, 2003

MMN to the Deviant Footstep



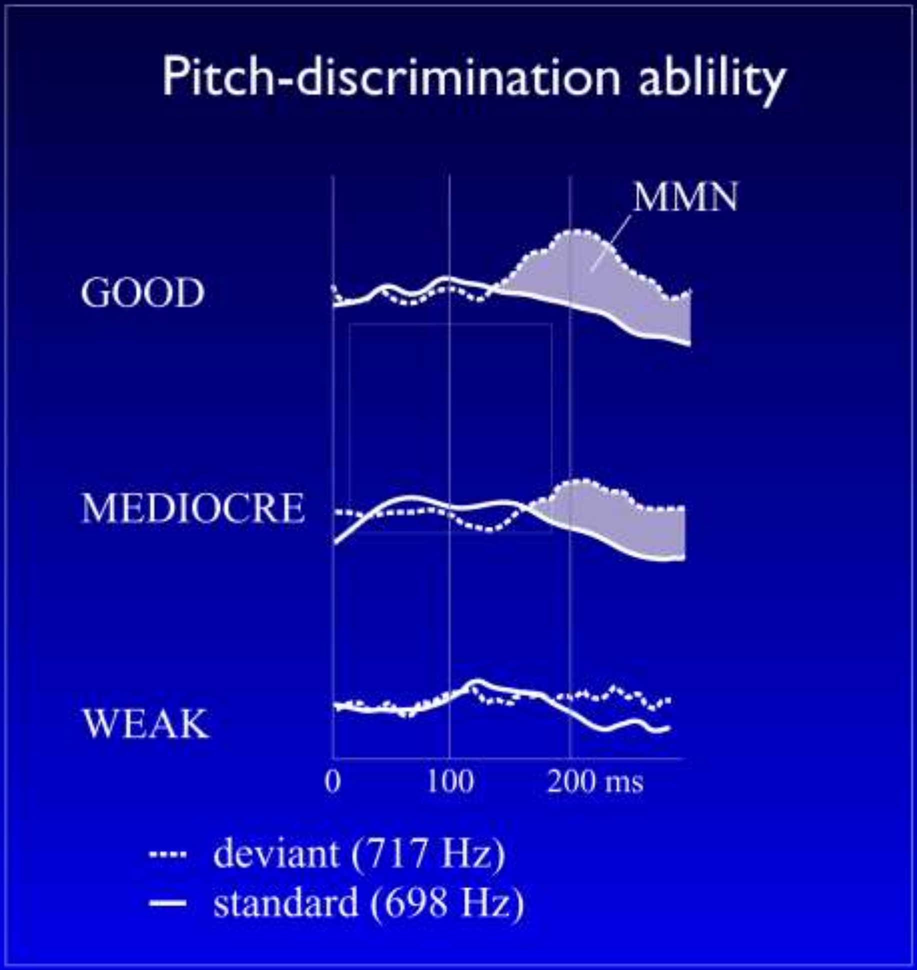
Winkler *et al.*, 2003

MMN to sound omission



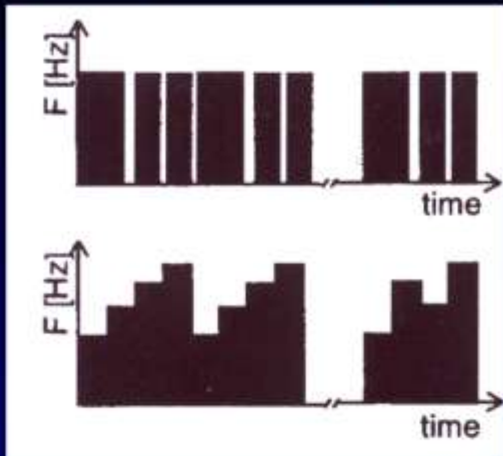
Yabe *et al.*, 1997

MMN as an objective index of sound *discrimination* opens a new dimension in evoked-response audiometry (ERA) previously able to index sound *detection* only.

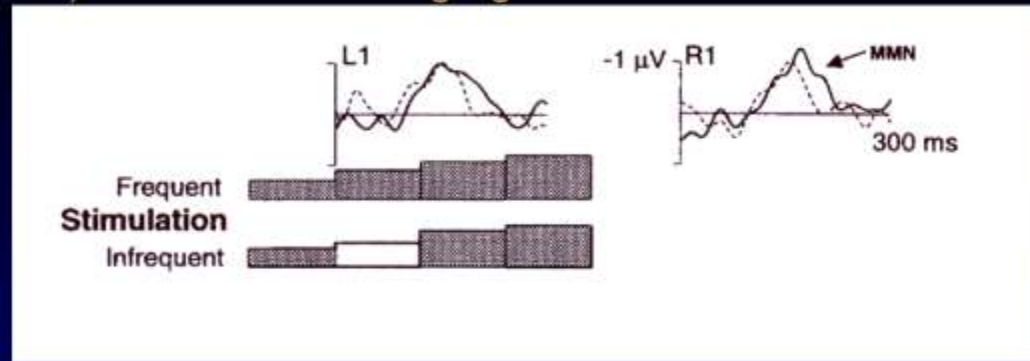


MMN as a function of behavioral pitch-discrimination accuracy. MMN (recorded in a separate reading condition) was larger in school children classified as "good" in a behavioral pitch-discrimination task (Seashore's test of musicality) than in those who were "mediocre" or "weak" in this task (Lang *et al.*,1990).

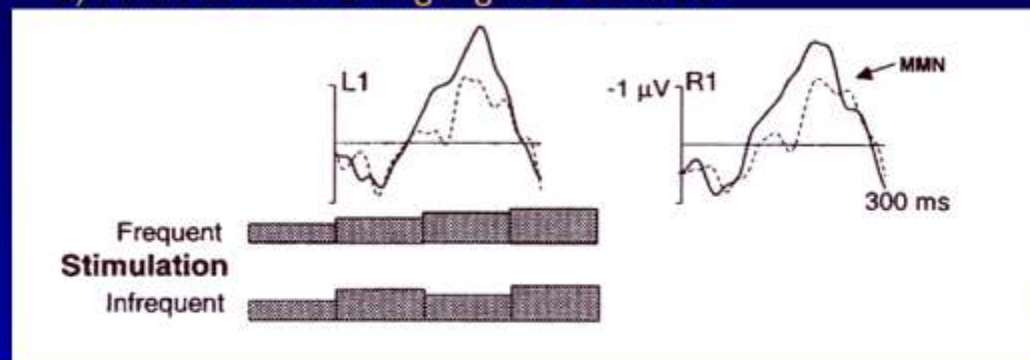
A) Examples of Musicality-test items



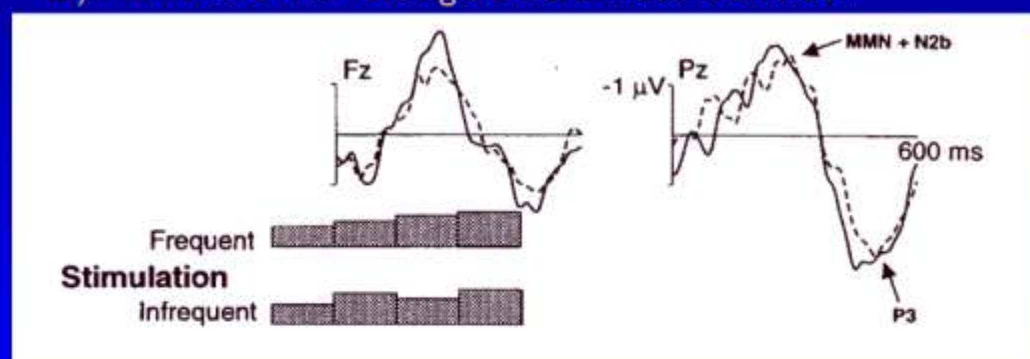
B) MMN to Order Change: Ignore Condition



C) MMN to Pitch Change: Ignore Condition



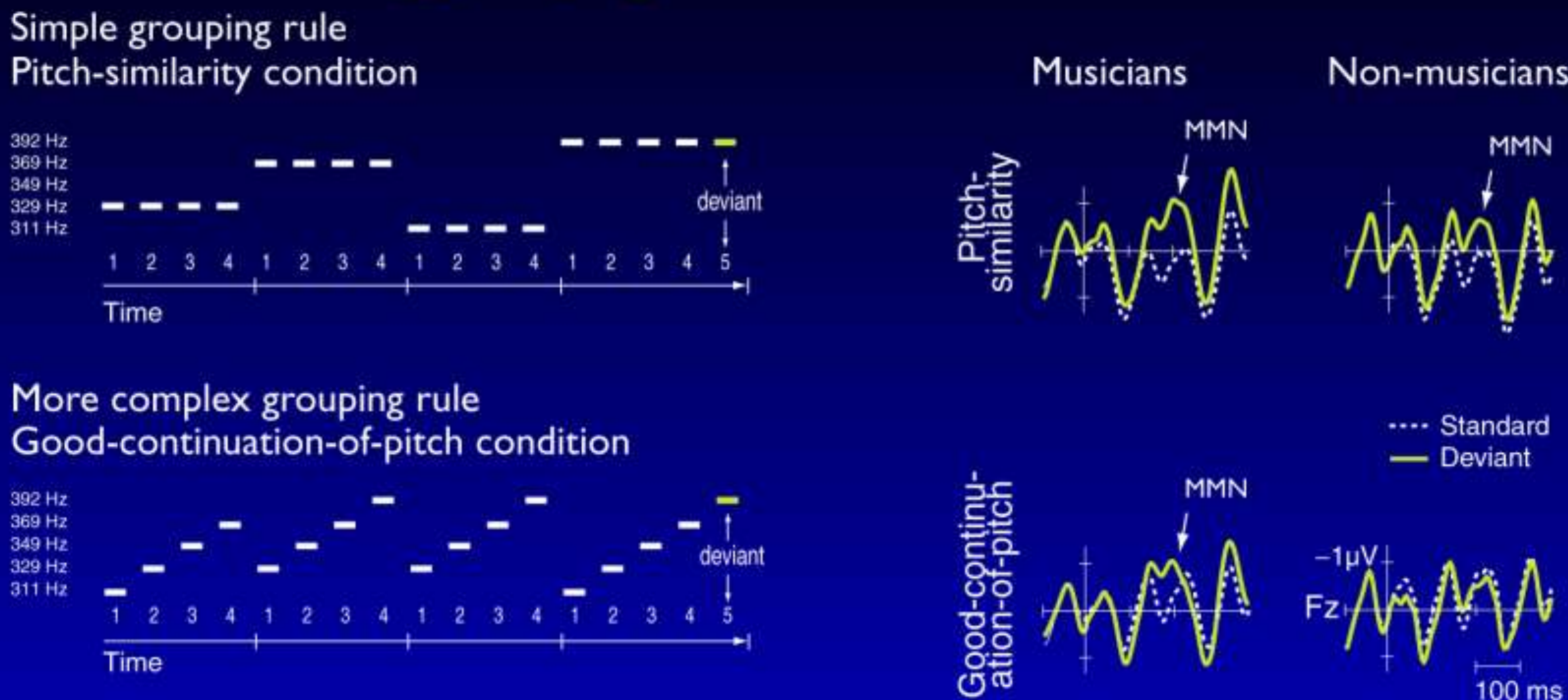
D) MMN to Order Change: Discriminate Condition



——— Musical
- - - - - Nonmusical

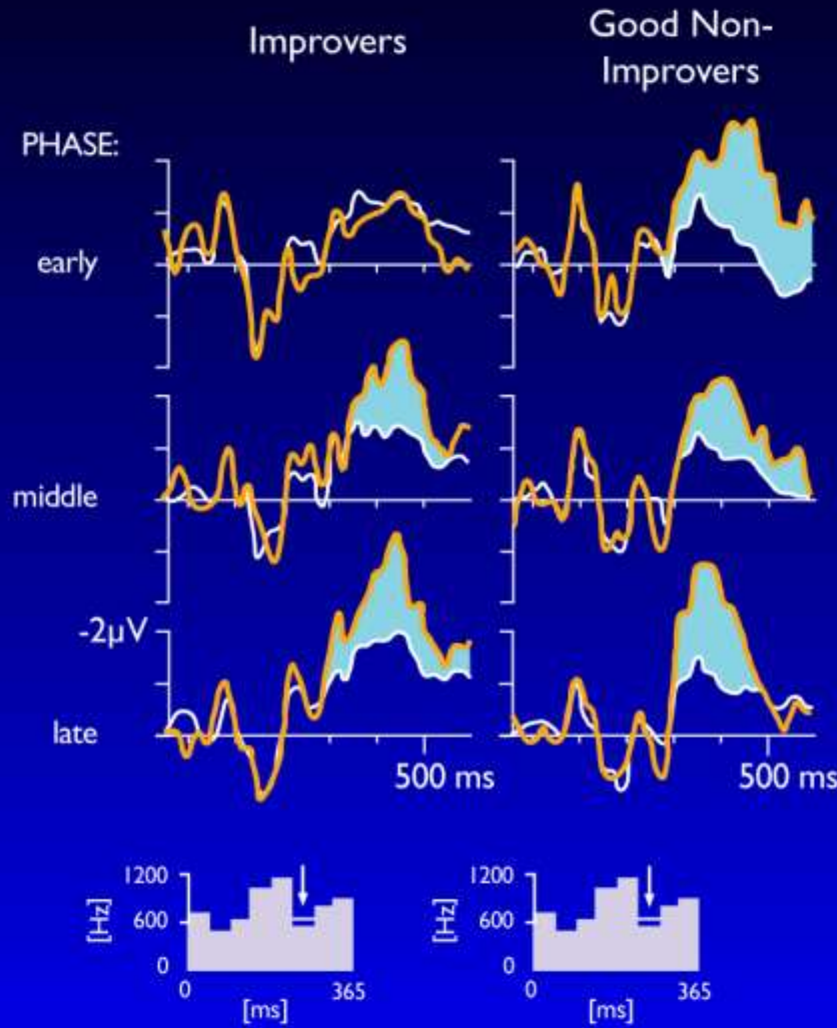
Tervaniemi *et al.*, 1997

Auditory grouping is more advanced in musicians



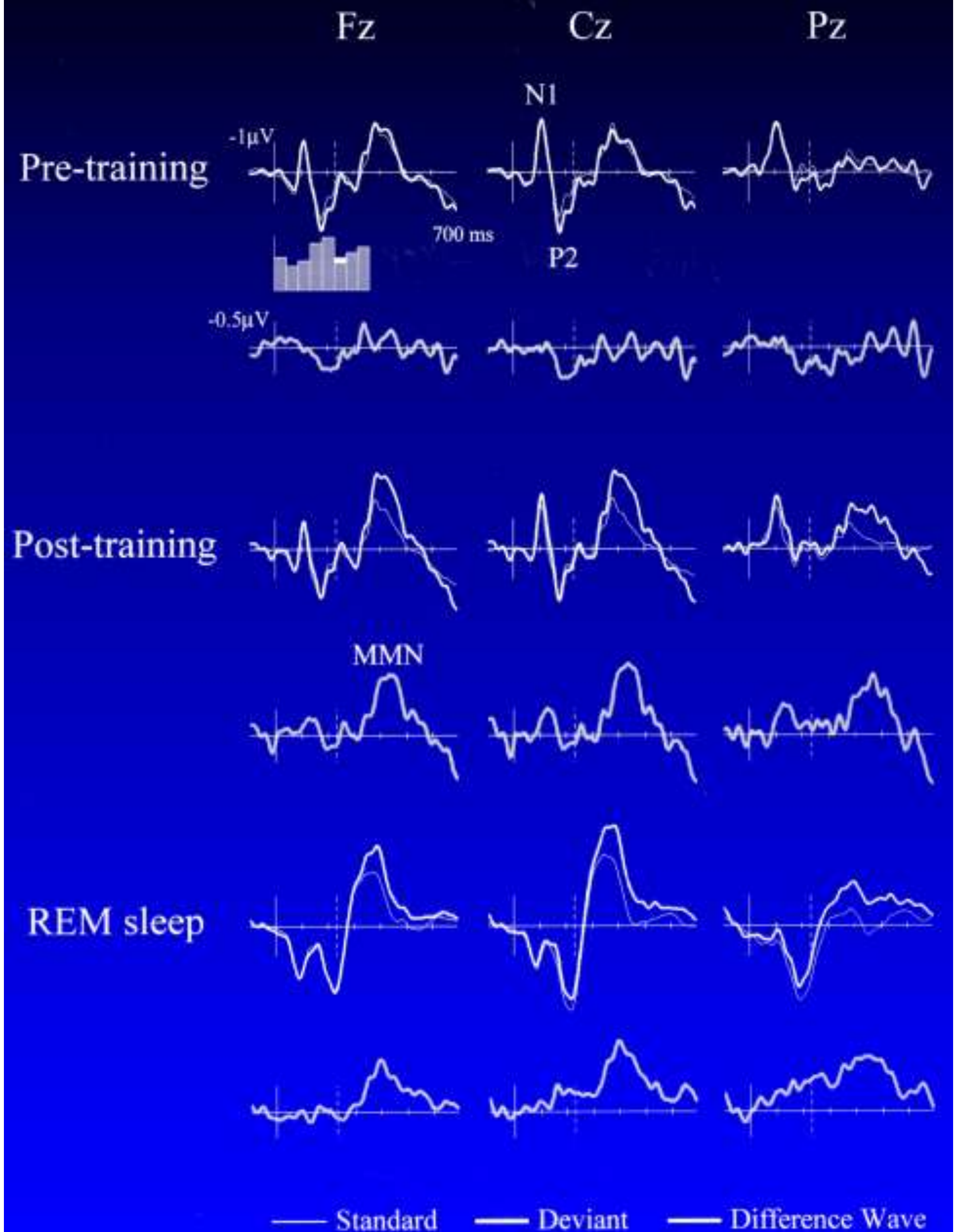
We presented two grouping rules of different complexity to non-musicians and musicians and measured the MMN to violations of the grouping rules to index grouping. Both non-musicians and musicians grouped the tones according to the easier rule. Only musicians grouped the tones according to the more difficult grouping rule. This group difference indicates that grouping is not solely universal and that it is more advanced in musicians (van Zuijen *et al.*, in press).

MMN as a function of discrimination training

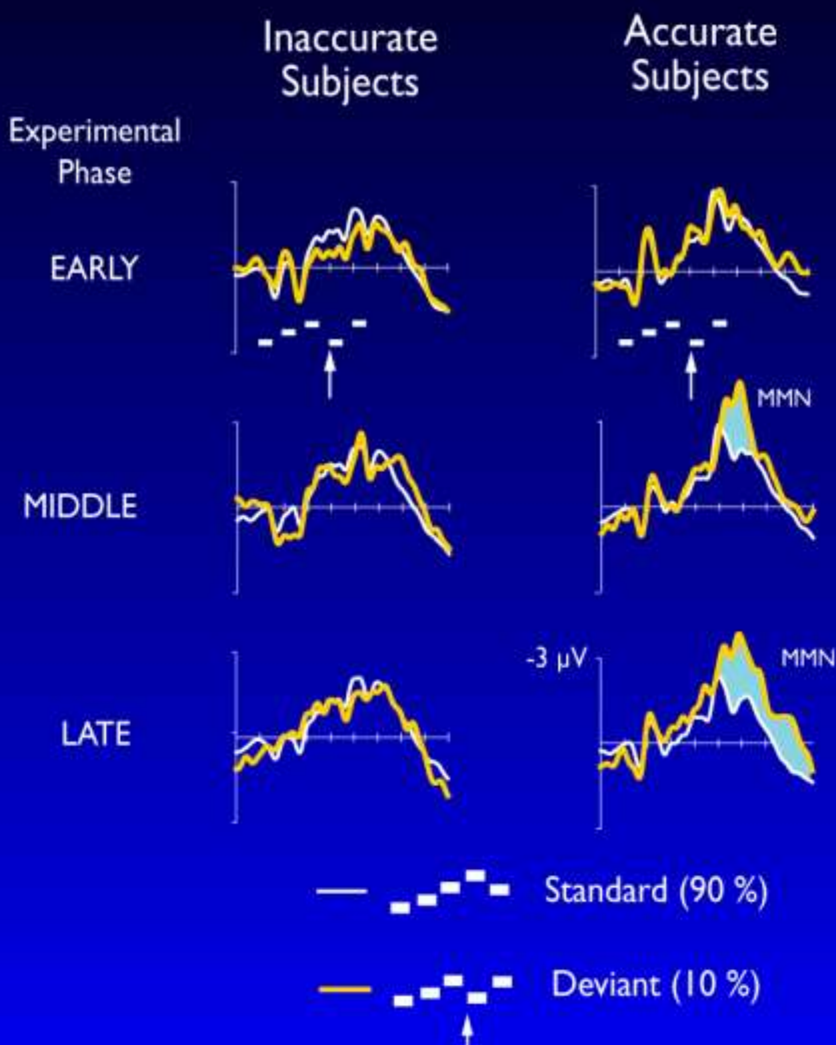


Näätänen *et al.*, TINS 1992

MMN training effect in REM sleep

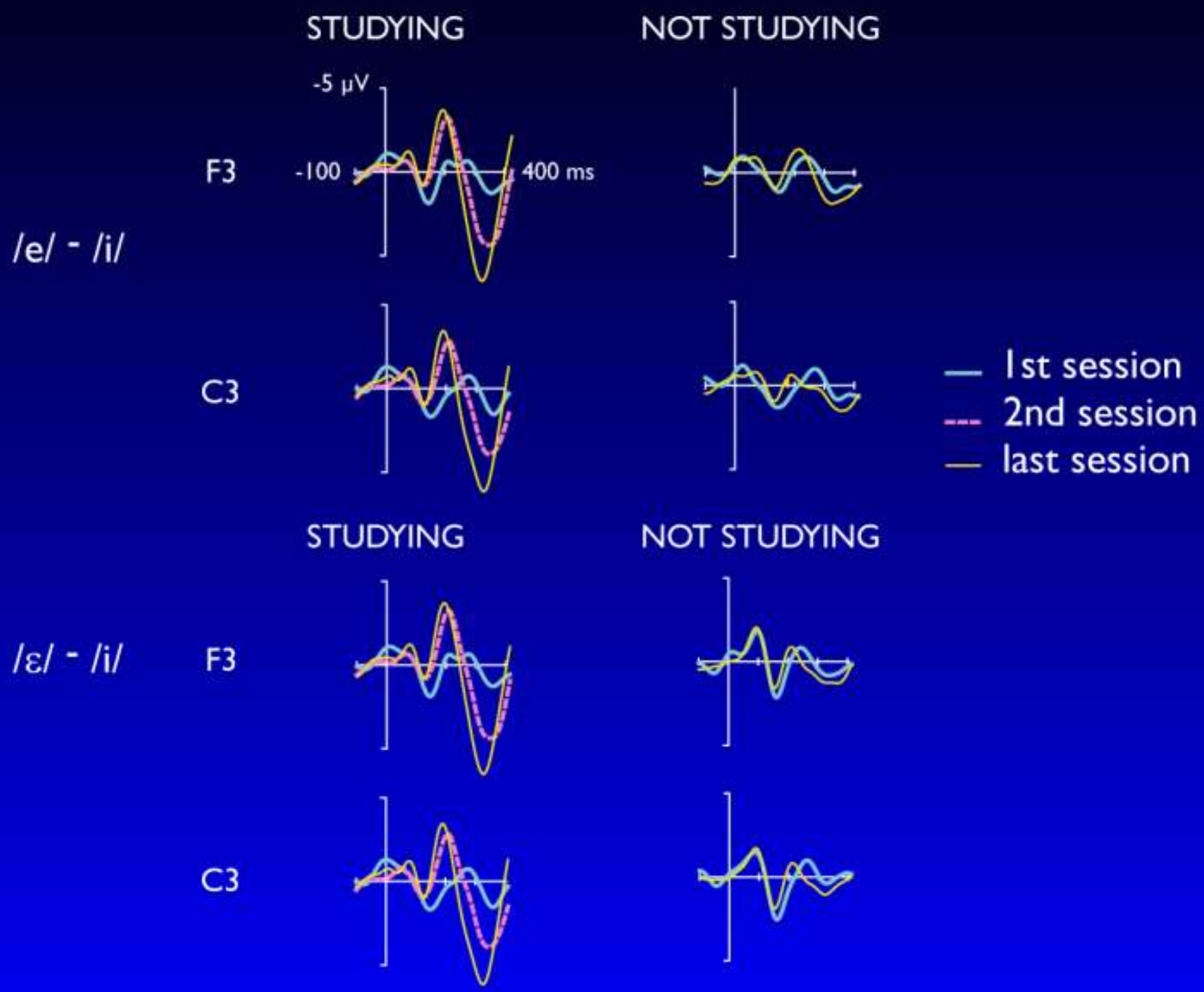


MMN as a function of training of an abstract pattern

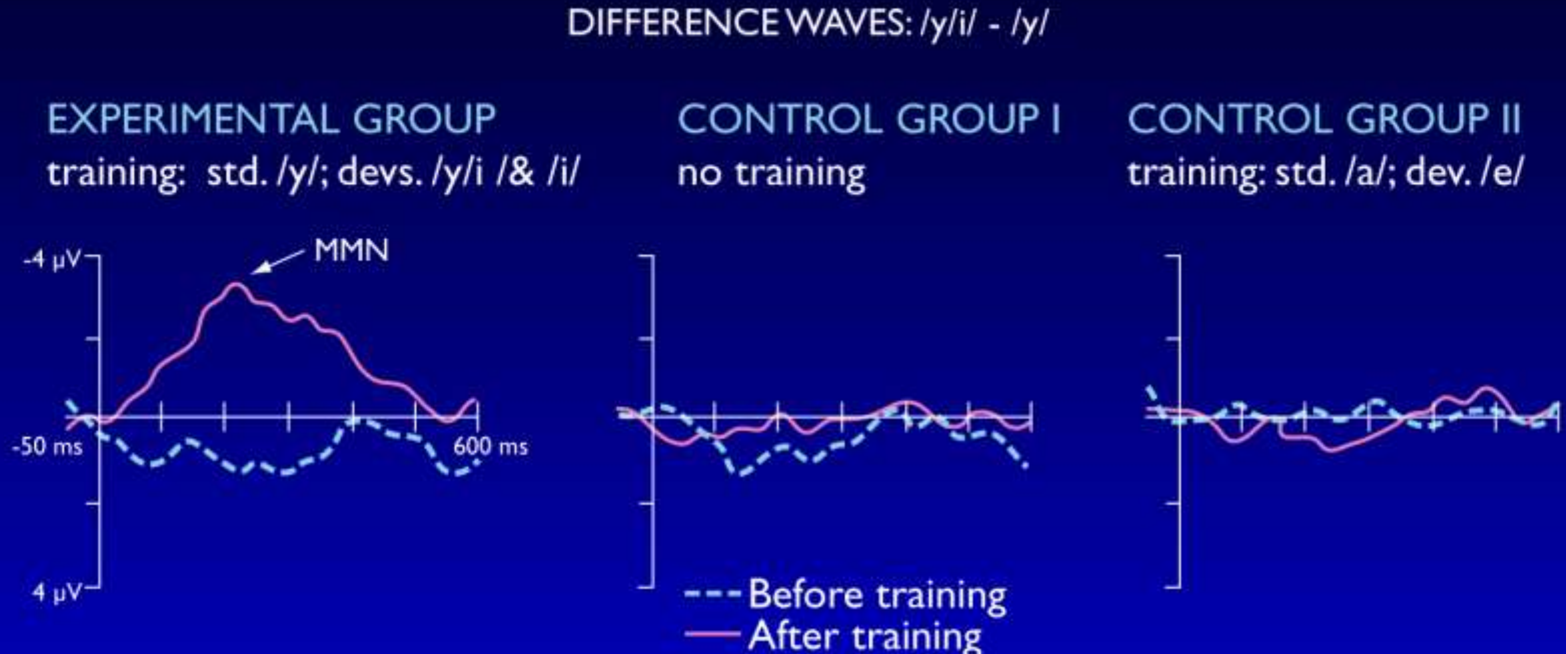


Tervaniemi *et al.* 2001

3-6 yr finnish children studying and not studying french

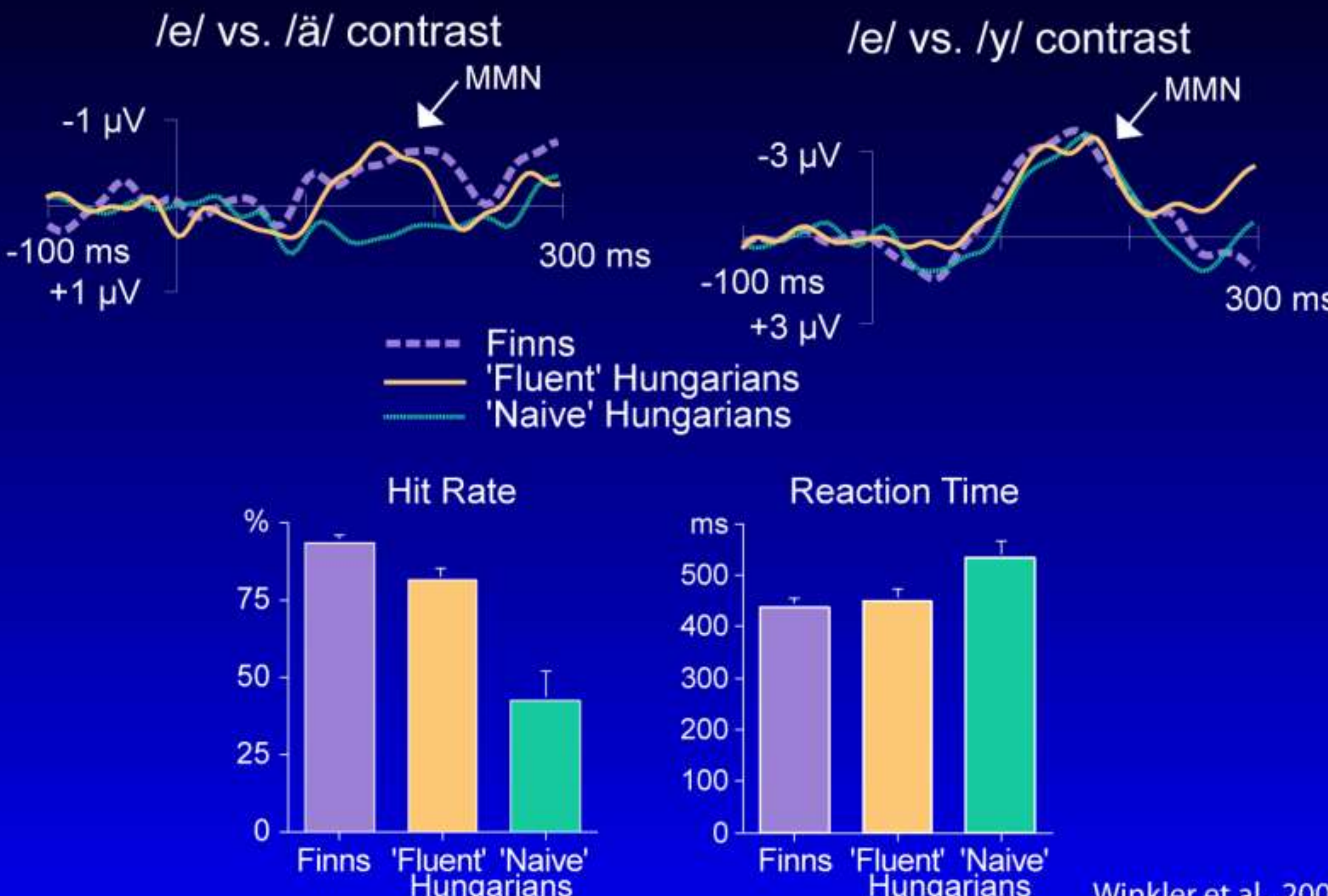


MMN shows phoneme-discrimination learning in sleeping newborns



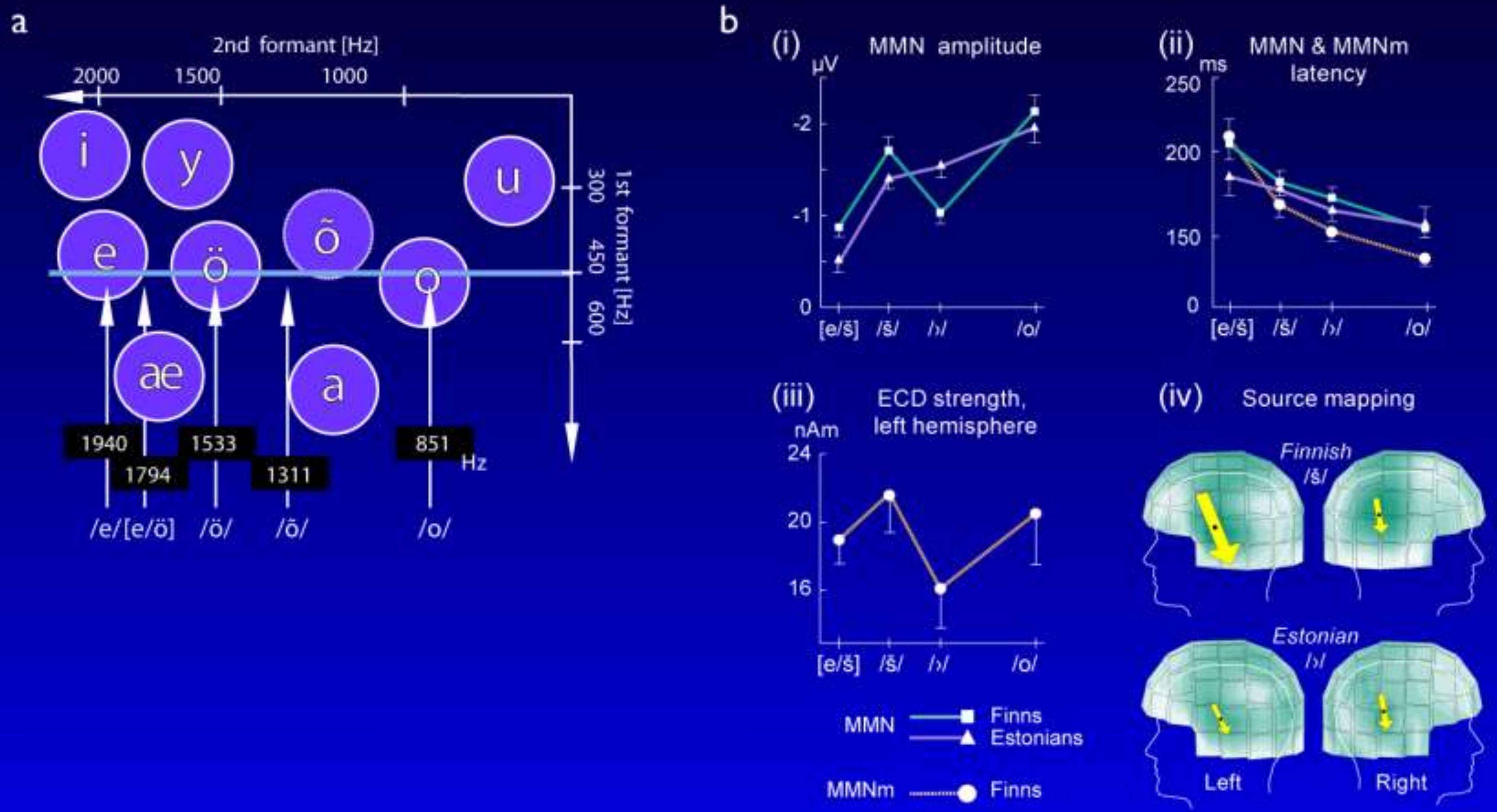
Left: There was no MMN for the /y/i/ - /y/ contrast in sleeping newborns in the evening (yellow line) but a large MMN was elicited in these infants (still sleeping) in the morning (orange line) after nocturnal training using these stimuli. **Middle:** In Control Group I, receiving no training, MMN was elicited neither in the evening nor in the morning. **Right:** In Control Group II, trained with /a/ - /e/ contrast, there was an MMN for the /y/i/ - /y/ contrast neither in the evening nor in the morning (Cheour *et al.*, Nature 2002).

MMN and Language Learning



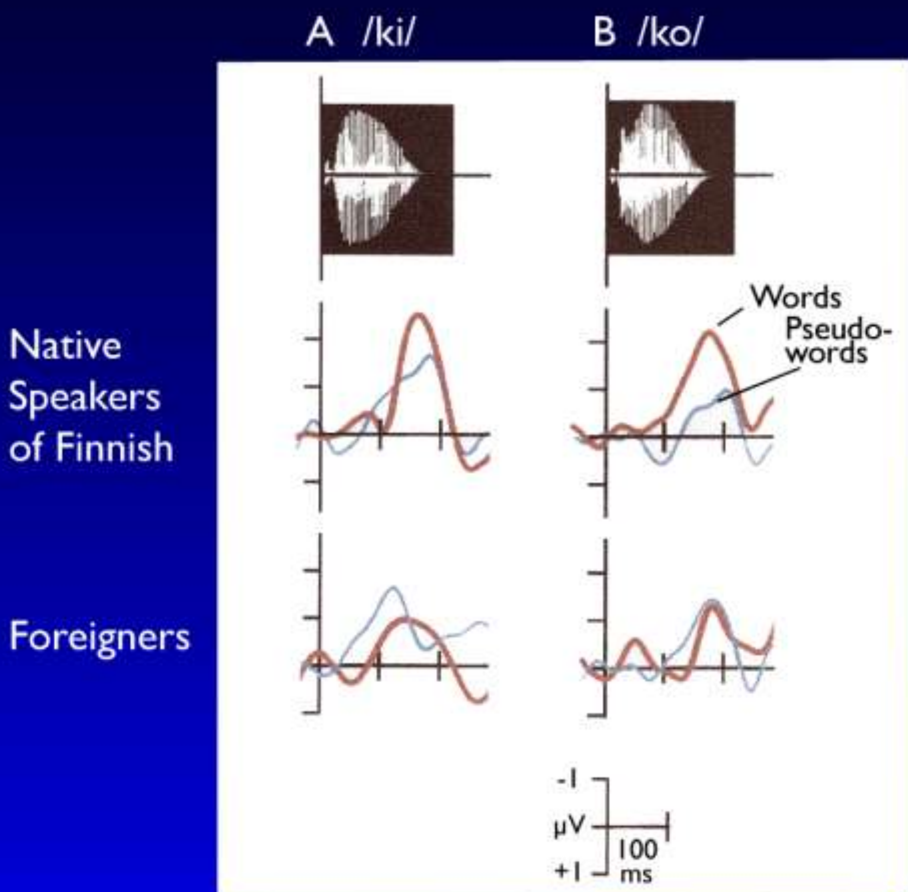
Winkler et al., 2003

Language-Specific Memory Traces



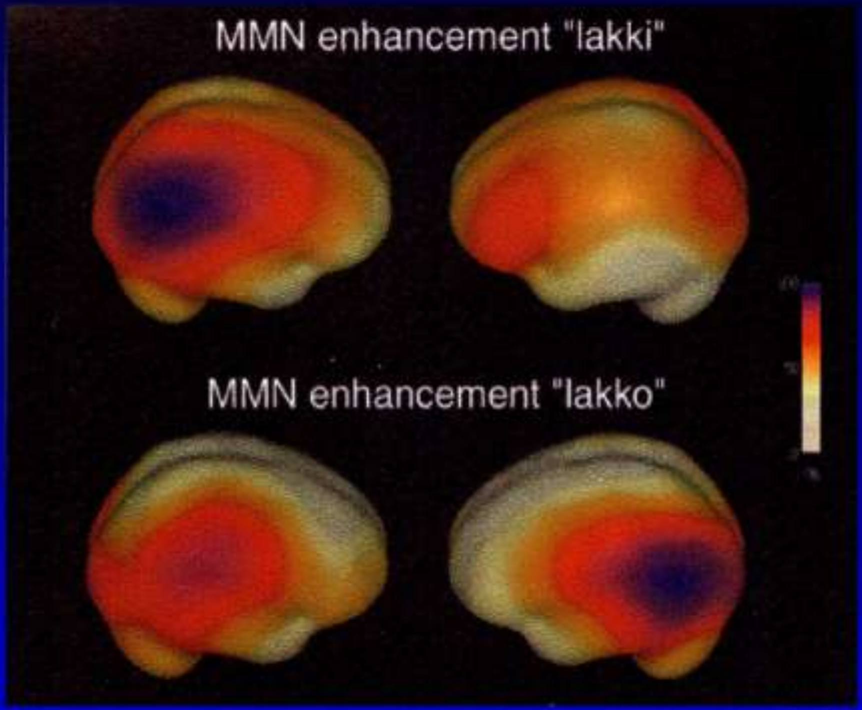
Näätänen *et al.*, Nature 1997

MMN reflects memory traces for words



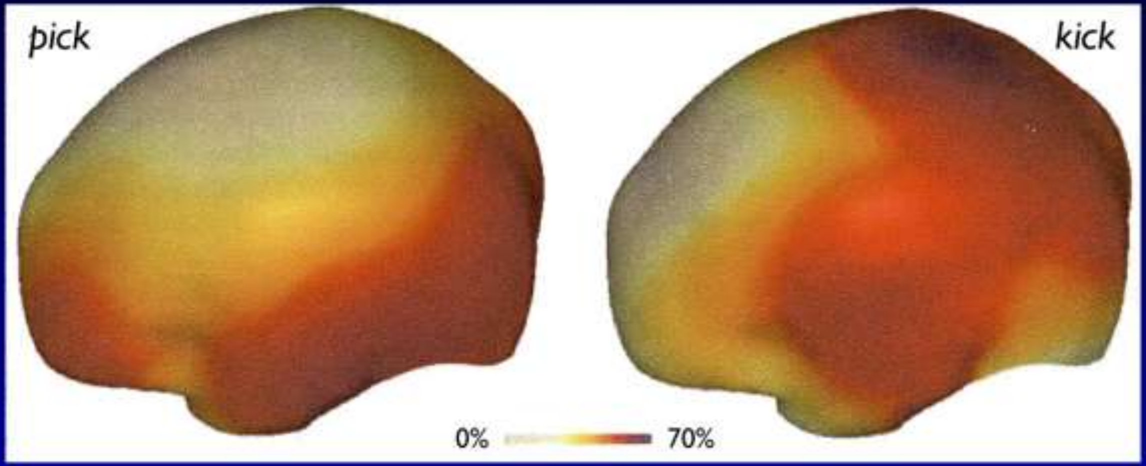
MMNs elicited by the critical syllables /ki/ (A) and /ko/ (B) when placed in a word context (red traces) and in a pseudo-word context (blue). The coustic waveforms of the stimuli which elicited the MMNs are shown at the top. Data from Finnish speakers are presented in the upper plots, those from foreigners appear at the bottom. A word-related MMN enhancement occured in Finnish speakers but not foreigners (Pulvermüller *et al.*, 2001).

Word-related MMN enhancement reflects semantic meaning



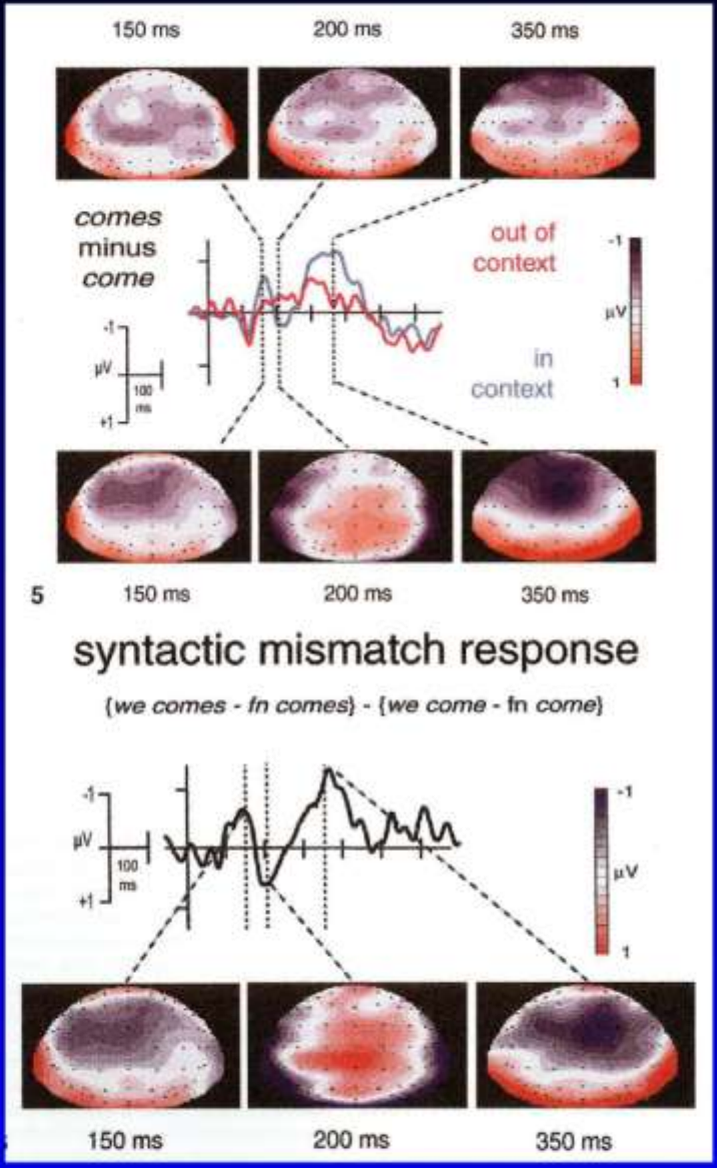
Minimum-norm current estimates of the distribution of the cortical sources underlying the maximal word-related MMN enhancements projected on a schematic gray matter surface. The top diagrams show the MMN enhancement for the word l*akki* and the diagrams at the bottom that for the word *lakko*. The color code represents the strengths of the estimated cortical sources in percent of the strongest source calculated for the relevant time interval (Pulvermüller *et al.*, 2004).

MMN for action words reflect semantic meaning



Minimum-norm current estimates of grand-average MMN responses evoked by the two action words (the respective peak latencies in event-related potentials were used for source-reconstruction). Response to the hand-related word stimulus (*pick*) showed a more lateral activation, whereas the leg-related stimulus (*kick*) produced also a focal dorsal source (Shtyrov *et al.*, 2004)

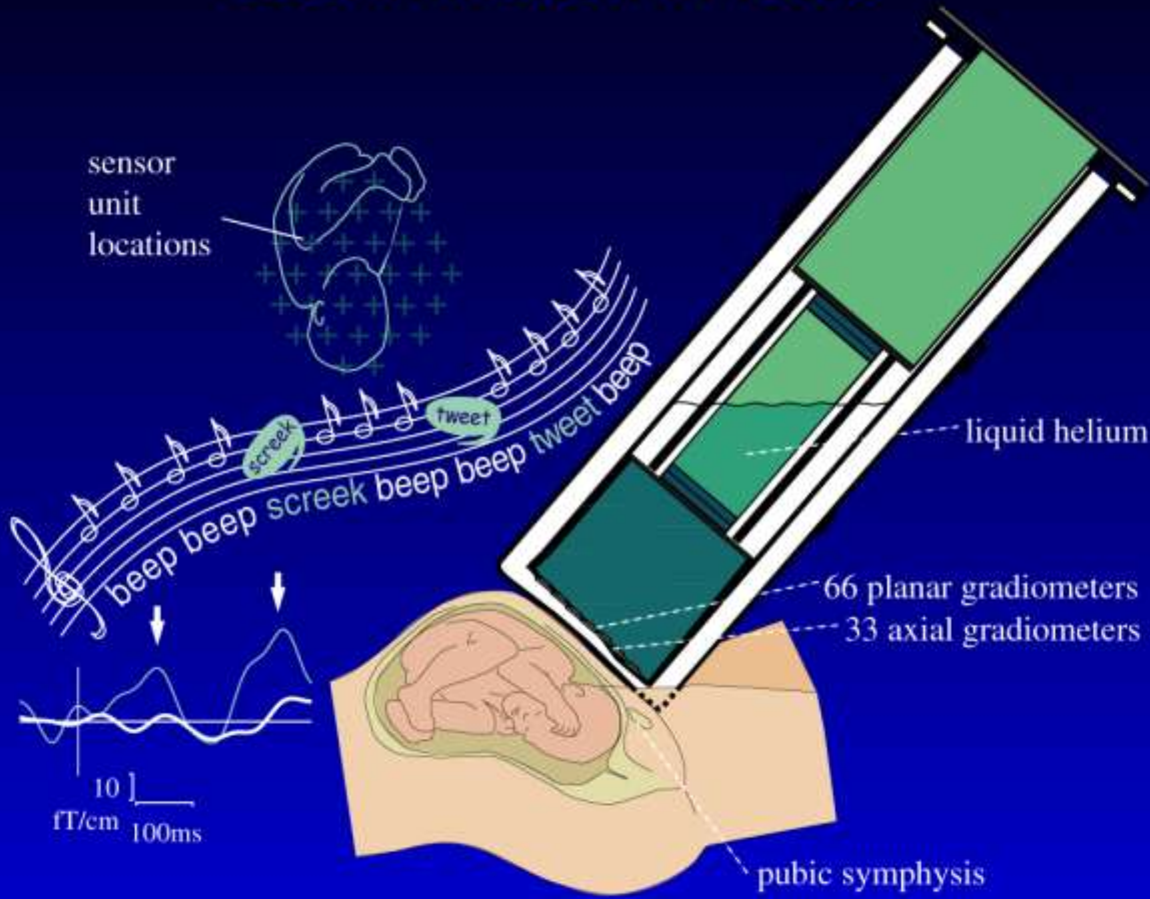
MMN to syntactic violation



The differences between the MMNs elicited by *comes* and *come* recorded at FCz are shown for the experiments where these words were presented out of context (after filtered noise; red curves) and in context (after the word *we*; blue curves). The maps illustrate the topography of the between-word difference at three critical time points, at 150, 200, and 350 ms after the divergence point. The most striking differences between the two difference curves are the enhanced negativities at 150 and 350 ms and the appearance of a brief central positivity around 200 ms in context.

Curves and maps illustrate the modification of the MMN in grammatical vs ungrammatical contexts after correction for between-word differences. The curves show event-related potentials recorded at FCz. The maps show the topography of the grammatically related MMN difference at three critical time points, at 150, 200, and 350 ms after the divergence point (Pulvermüller *et al.*, 2003).

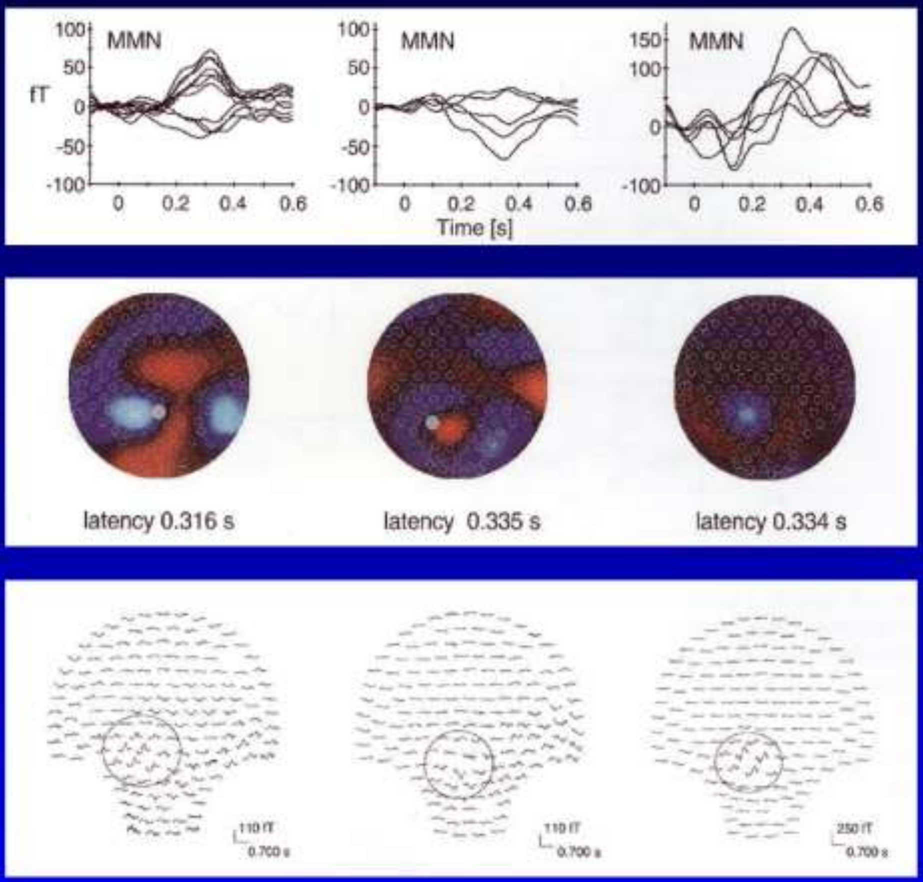
MMNm shows auditory discrimination in fetus



MMN recorded magnetically (MMNm) from a fetus in the womb demonstrates sound discrimination in fetus (Huotilainen *et al.*, 2005).

MMN to frequency change in a complex tone in a fetus at 33 and 36 weeks and 10 days after birth

Fetus 33 week Fetus 36 week Newborn 10 days

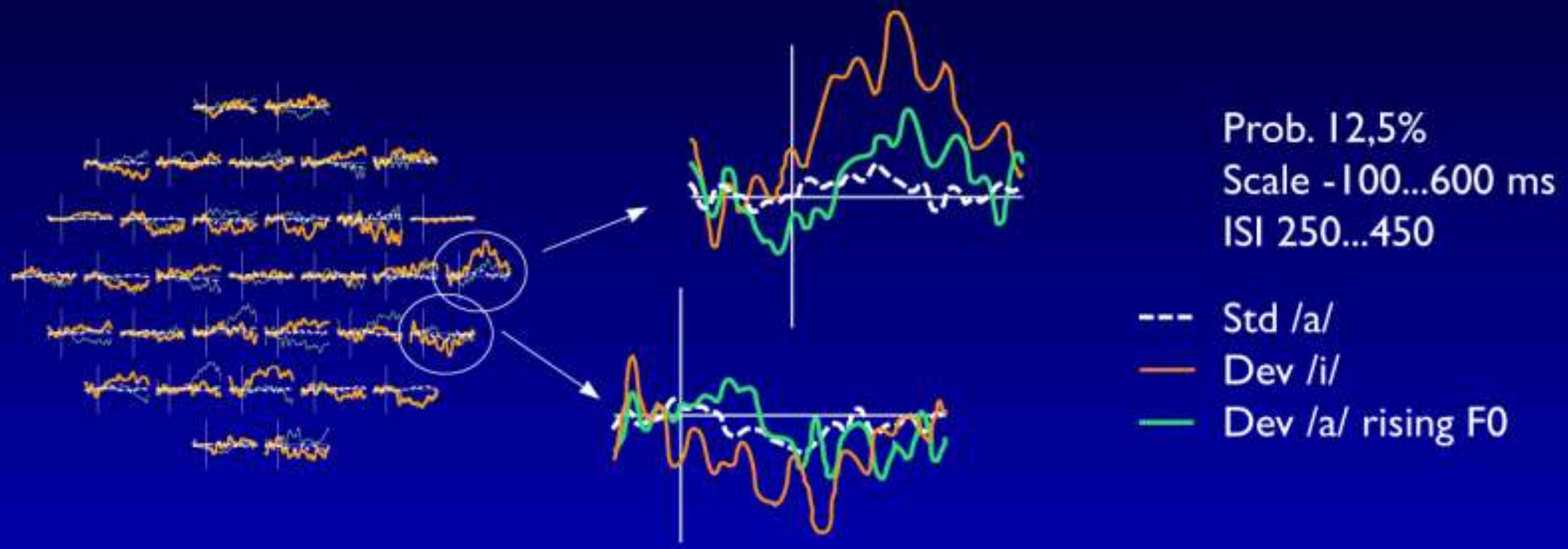


Upper panel, channels with responses for a fetus at 33 week and 36 week of gestation and 10 days after birth.

Middle row, magnetic fields distribution of the MMN responses, corresponds to the maximal peaks of the responses. The circle indicates the location of fetal head position.

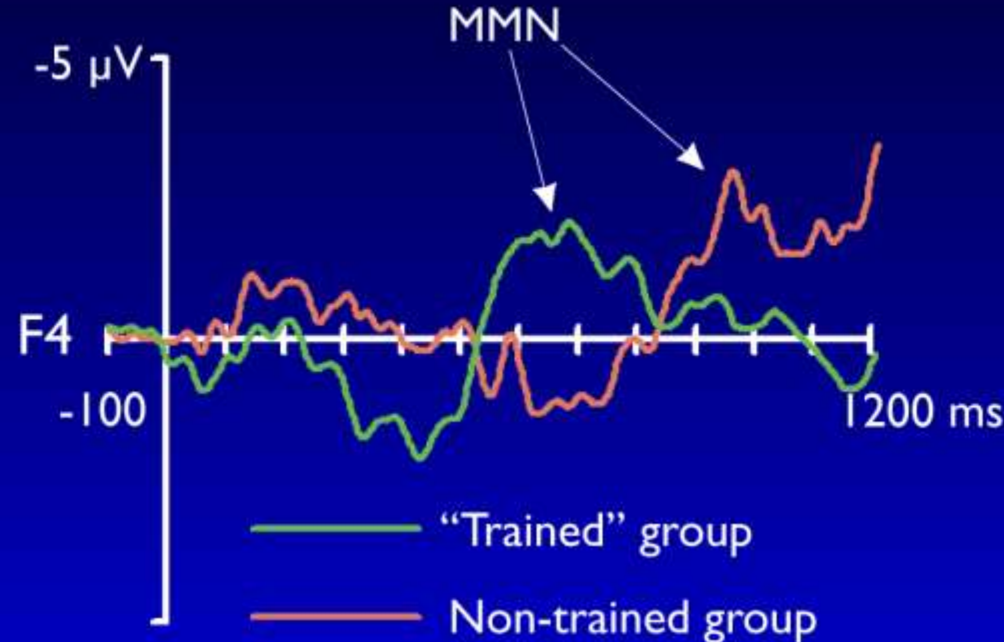
Bottom row, the time traces for each sensor for MMN response (Draganova *et al.*, 2005).

A change in a phoneme evokes a magnetic response in a healthy fetus at 36 weeks



Magnetic brain responses (left) of a 36-week-old healthy human fetus were recorded to phoneme /i/ (red line) and phoneme /a/ with rising intonation (green line) presented rarely among repeated phonemes /a/ (white line). The two magnetic channels enlarged on the right show that both of these changes were detected by the fetus (Huotilainen *et al.*, in prep.).

Fetal language learning



Huotilainen *et al.*, in prep.

Brain indices of fetal learning

Music: fetuses were taught the Twinkle twinkle little star -melody during the last trimester of pregnancy. At birth the P350 response amplitude differed between the groups and at four months the learning group had an MMN.

Original melody

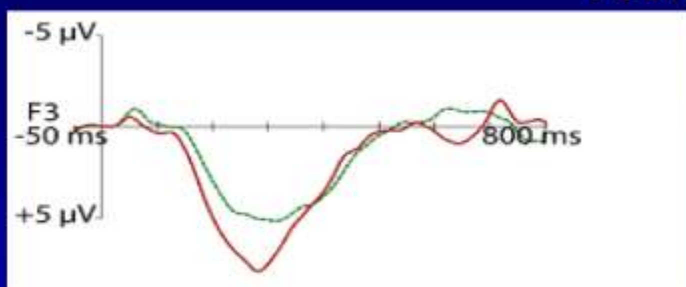
Modified melody

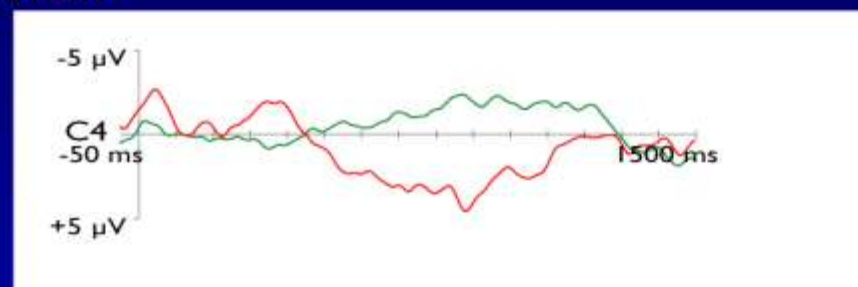
Speech: fetuses were taught thai phrases during the 3. trimester of pregnancy. At birth and at 4 mo, infants had an MMN to modified phrases with a rising F0 contour.

Standard

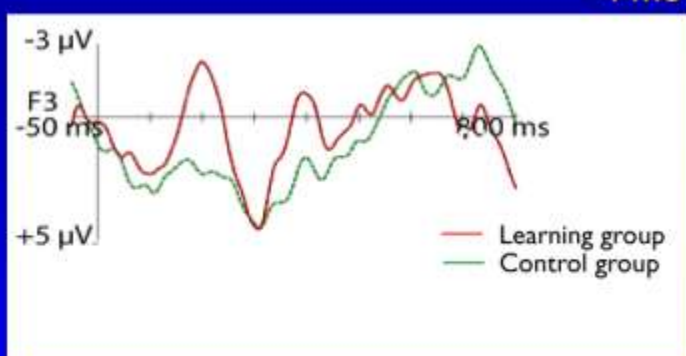
Deviant

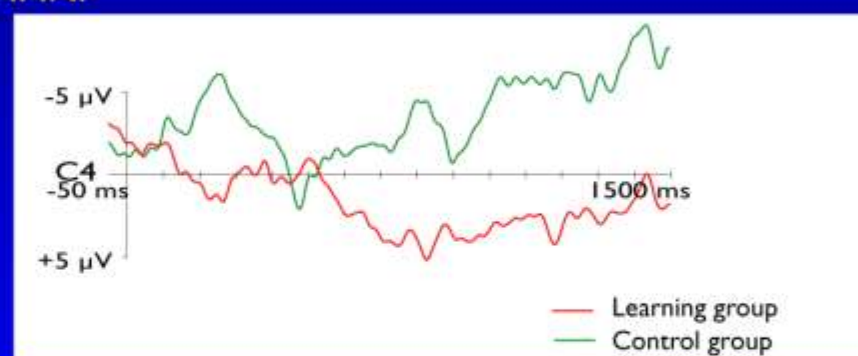
At birth: P350





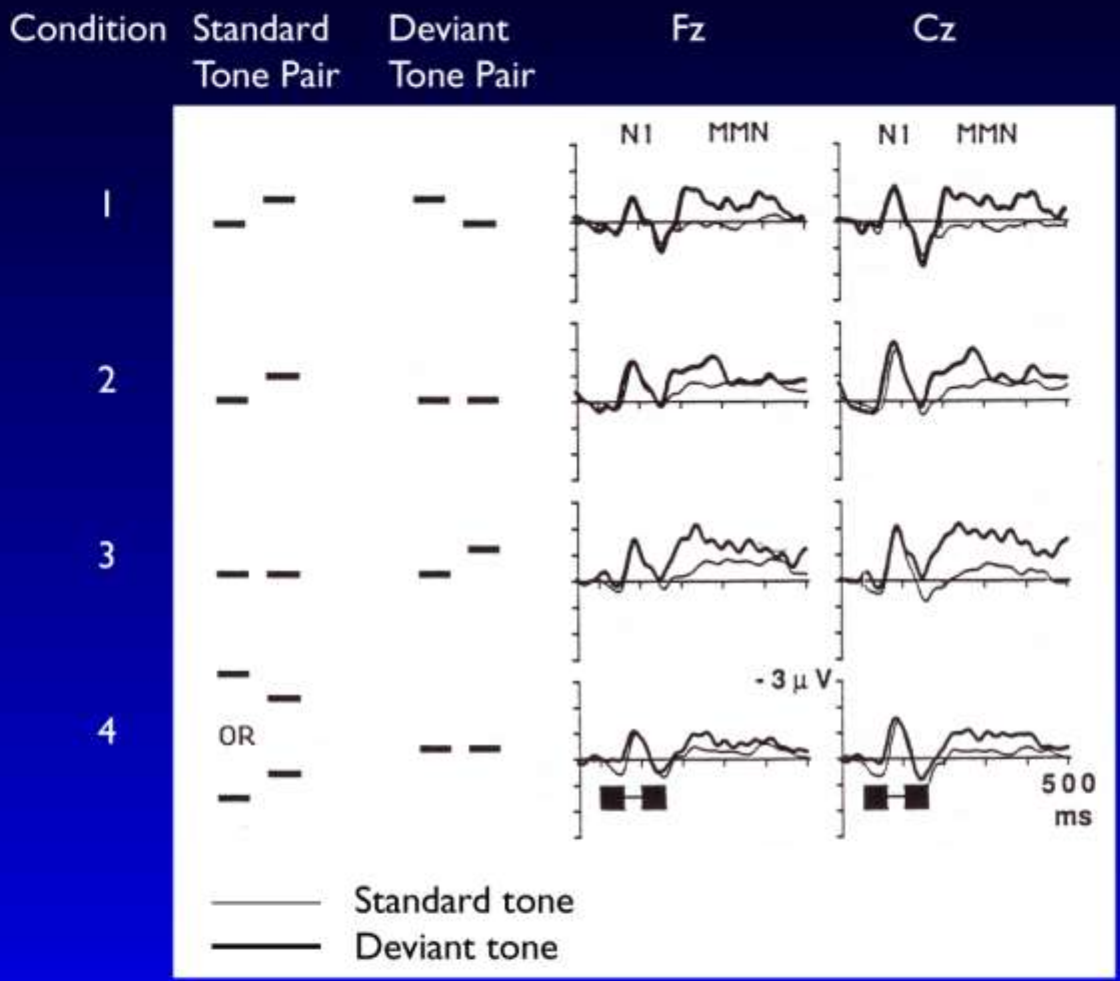
4 mo MMN:





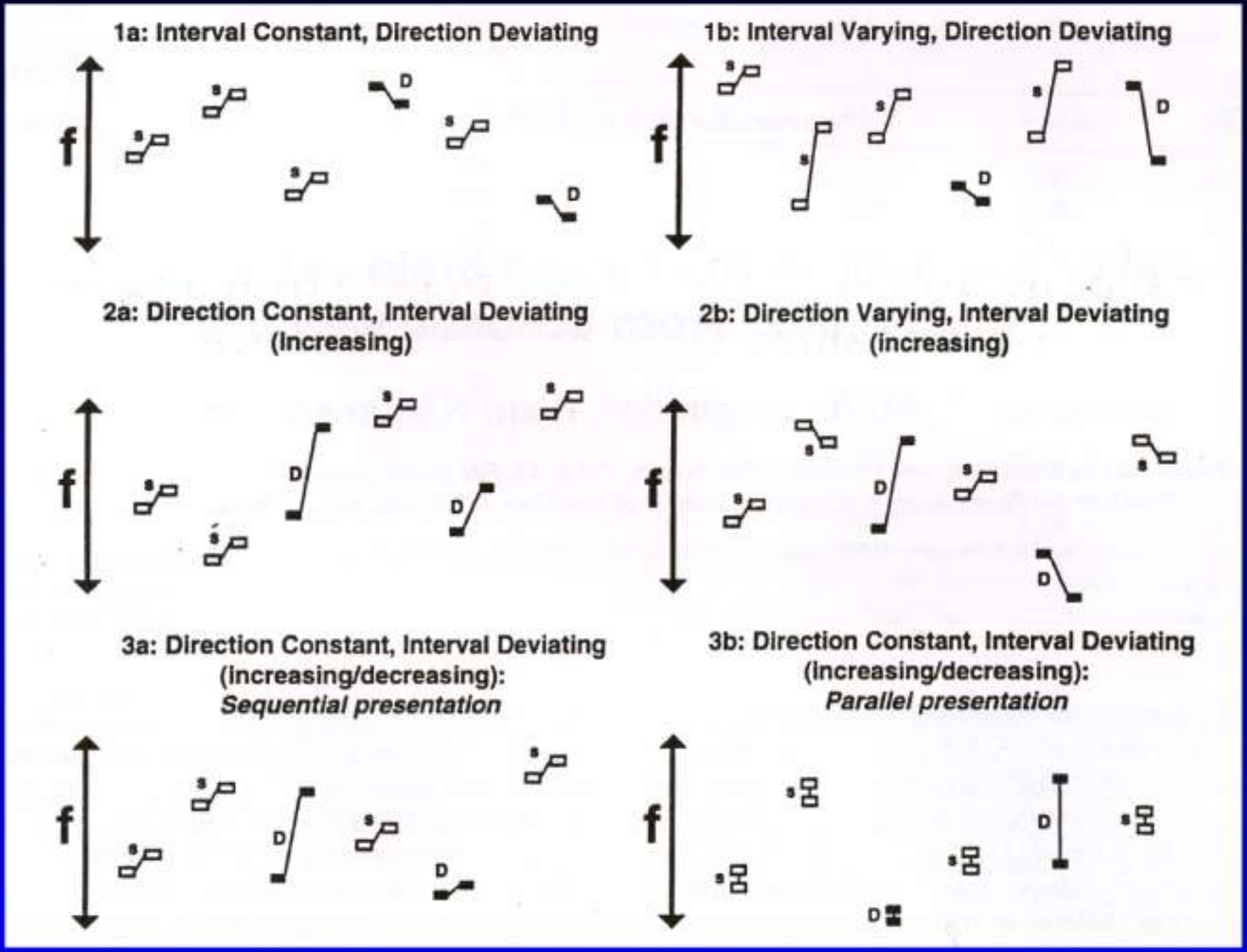
Partanen *et al.*, in prep & Huotilainen *et al.*, in prep.

MMN to tone pairs



Saarinen *et al*,,1992

Abstract patterns: Stimuli



Paavilainen *et al.*, 1999

MMN to changes in abstract patterns

Standard Direction: ascending
Deviant Direction: descending

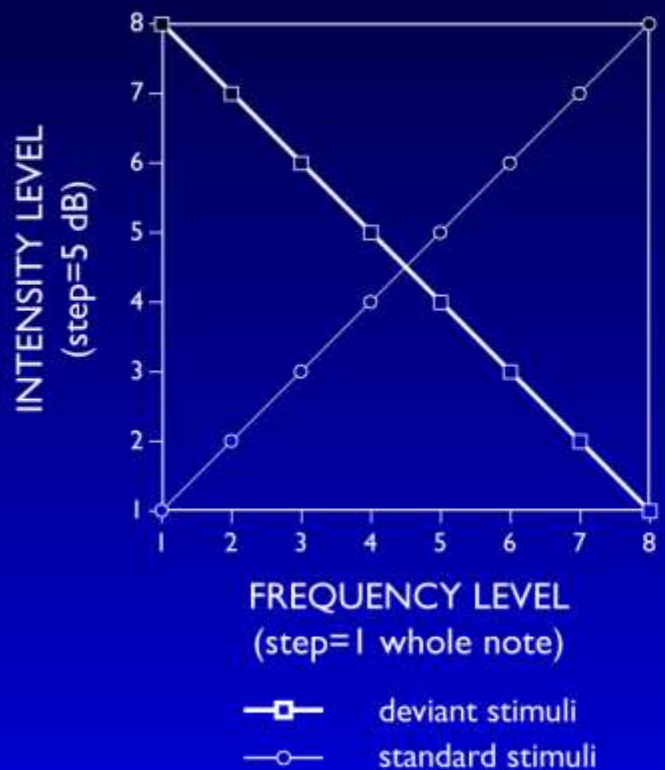
Standard Interval: 1 step
Deviant Interval: increasing 2-10 steps

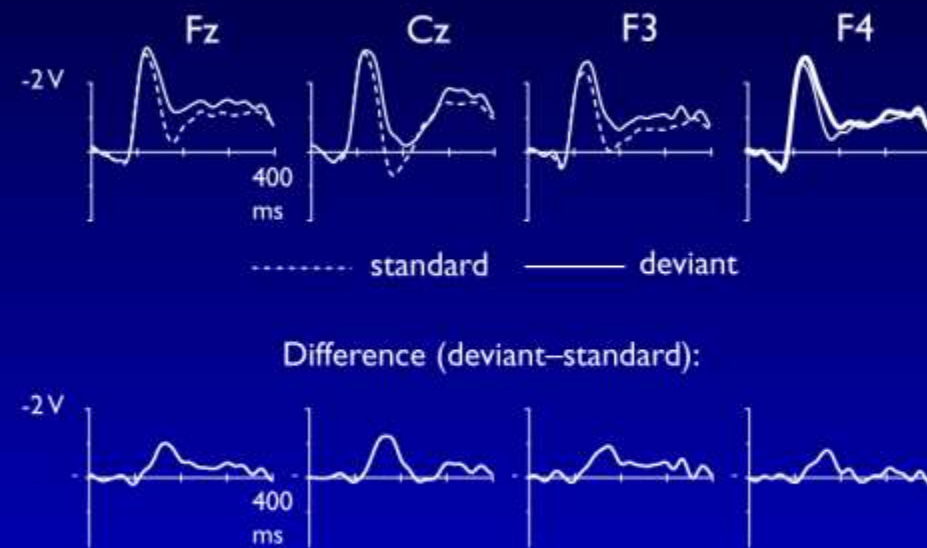
Standard Interval: 5 steps
Deviant Interval: decreasing 2 or 3 steps

Standard Interval: 5 steps
Deviant Interval: increasing 7 or 8 steps

Paavilainen *et al.*, 1999

MMN to frequency/intensity conjunction deviants

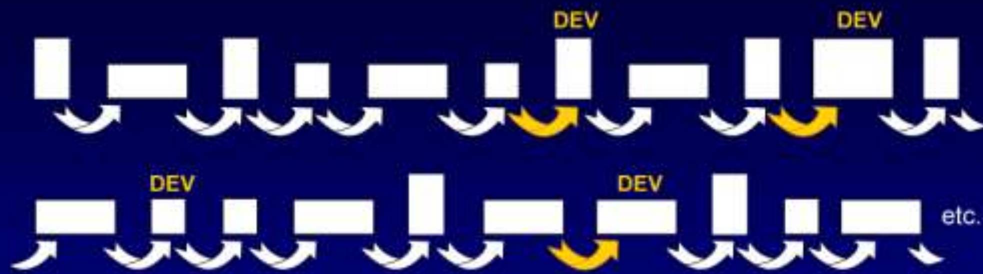




Paavilainen *et al.*, 2001

Auditory system predicts unconsicously

Stimuli



DEV=deviant stimulus

= long low stimulus

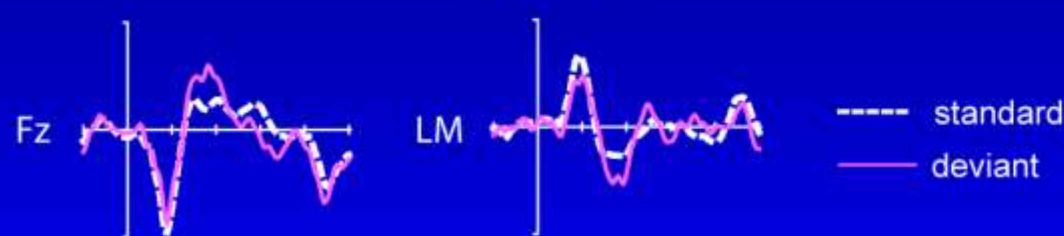
= short low stimulus

= long high stimulus

= short high stimulus

Short tone predicts low frequency, long tone predicts high frequency

Results

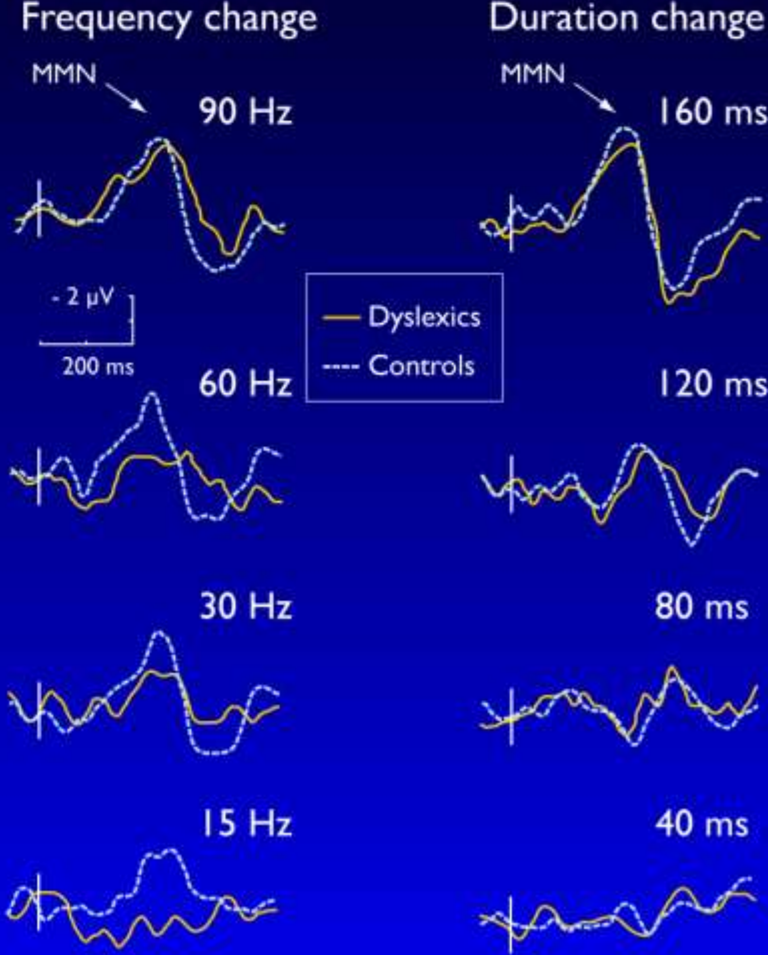


Paavilainen et al., in prep.

STM TRACE (MMN to violation of activated trace)

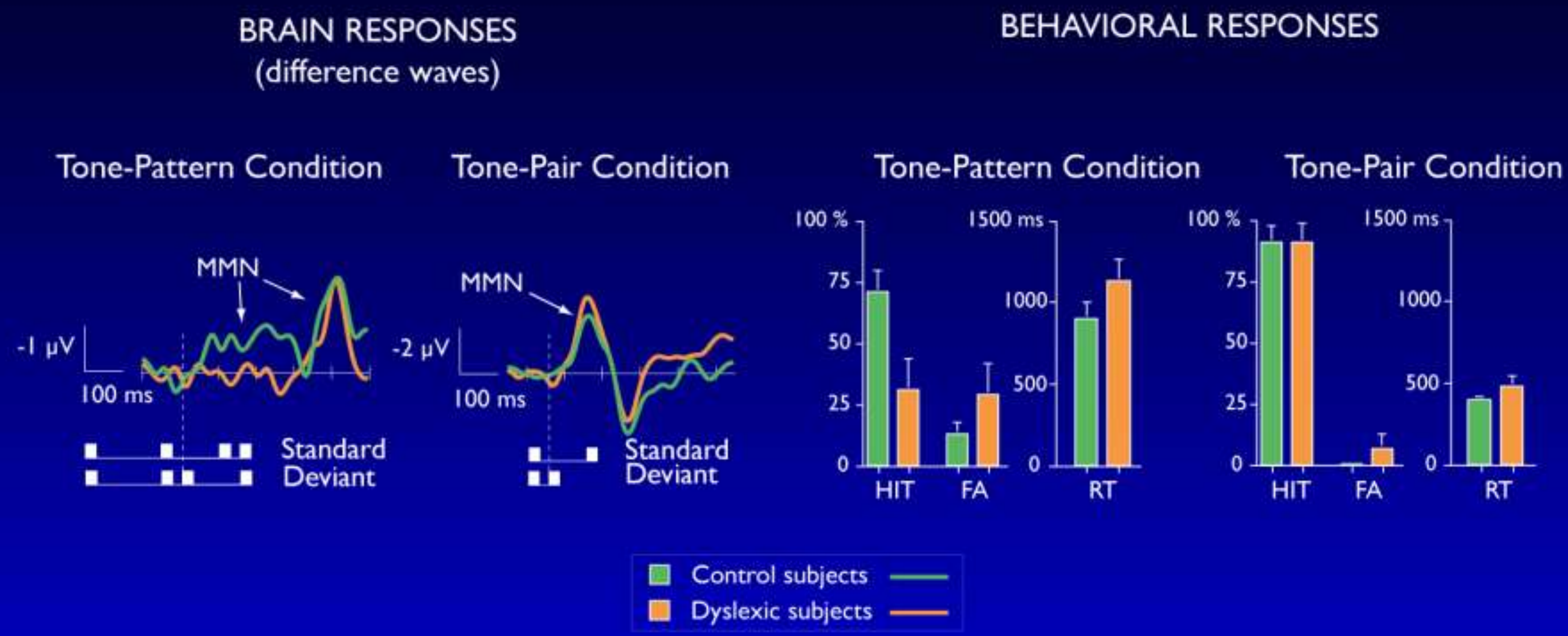
- Duration 10 s
- Formation attention independent
- Represents auditory events
- Corresponds to contents of perception
- In case of varying standards, may represent the trend or rule of this variation (”sensory-level intelligence”)
- MMN facilitated by previous LTM trace corresponding to the standard

MMN shows deteriorated frequency but normal duration processing in dyslexics



MMN (in an ignore-sounds condition, subjects performing a visual motion detection task) as a function of frequency change (left) and duration change (right) in dyslexic adults and controls. With a large frequency change (90 Hz; standards 1000 Hz), there was no MMN difference between the groups, whereas MMN vanished much sooner in dyslexics than controls with a decreasing frequency change. For duration change, in contrast, no group difference in MMN could be found for any level of duration change (Baldeweg *et al.*, 1999).

MMN shows deteriorated temporal processing in adult dyslexics

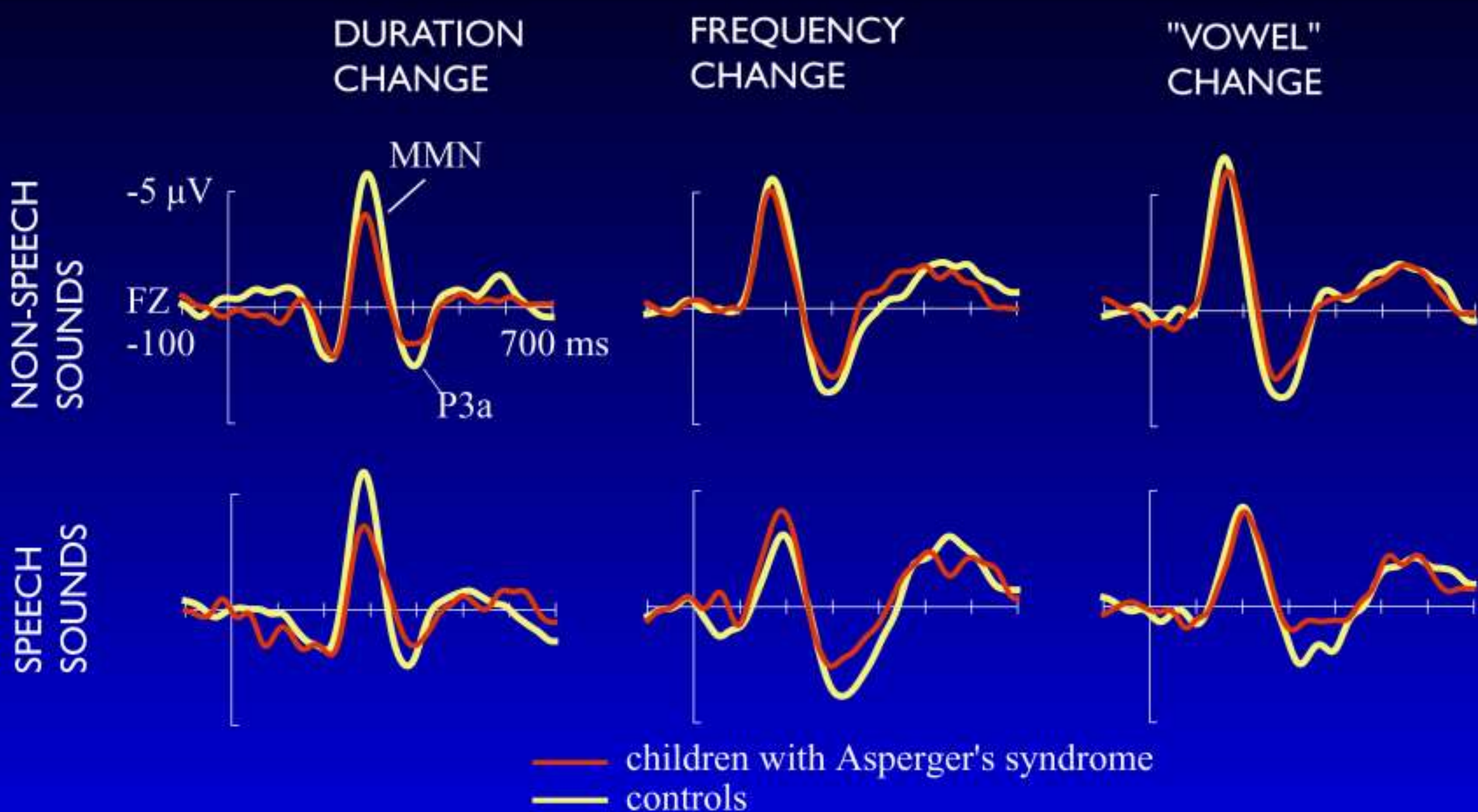


In Tone-pair condition, MMN to the shortening of the tone interval within the tone pair was similar in adult dyslexic and control subjects reading a book. Consistent with this, the behavioral discrimination of this change (studied in a separate condition) was equally good in the two groups. In contrast, when 2 extra tones were added, one before, and the other after the tone pair, then the shortening of the within-tone pair interval elicited no MMN in dyslexics, whereas it elicited a distinct MMN in controls. Consistent with this, for dyslexics, the discrimination of the deviant tone pattern was very difficult. (The later MMN in the leftmost figure, showing no inter-group difference, was elicited by stimulus omission in the end of the stimulus pattern, due to moving the third tone earlier in time.) (Kujala *et al.*, Psychophysiology 2000, Special Report.)

MMN shows the improvement of sound processing as a result of audio-visual training in dyslexic children

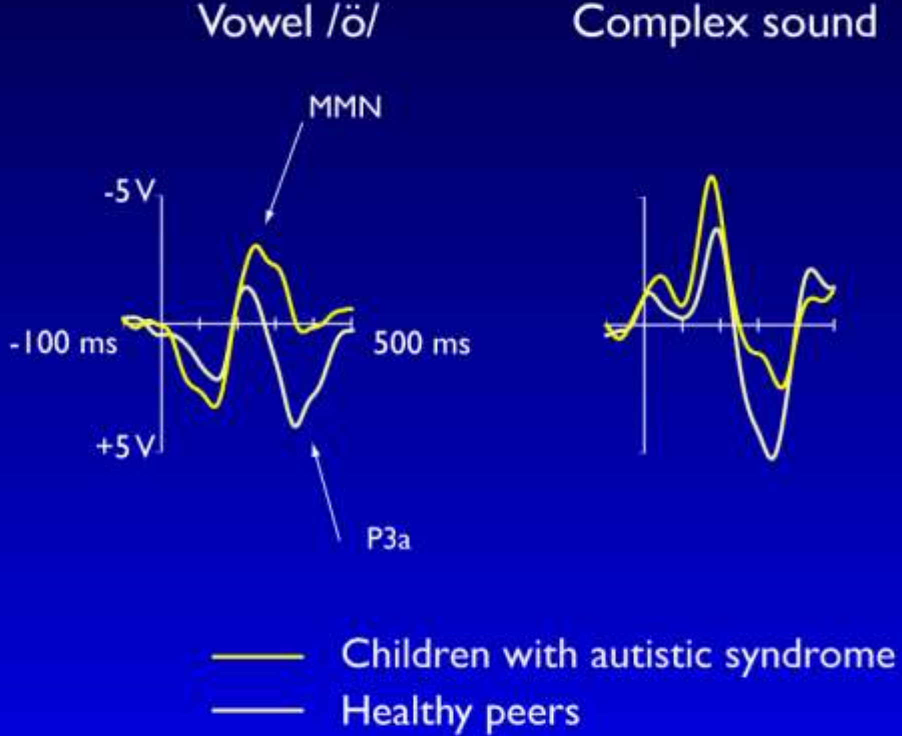
MMN to order change in a tone pair was quite small and of similar amplitude in two matched groups of 7-yr. old dyslexic children (top left) before audio-visual training but it was considerably enhanced in amplitude in the group that received training (Karma, 1999) lasting 7 weeks (20 min/week) (top right). Importantly, the improvement in reading accuracy (bottom left) and speed (bottom right) was much faster in the trained than in the un-trained group. Furthermore, the magnitude of the MMN amplitude increased by training correlated with the magnitude of improvement of the reading performance (Kujala *et al.*, PNAS 2001).

MMN shows deficient sound-duration perception in Asperger's syndrome



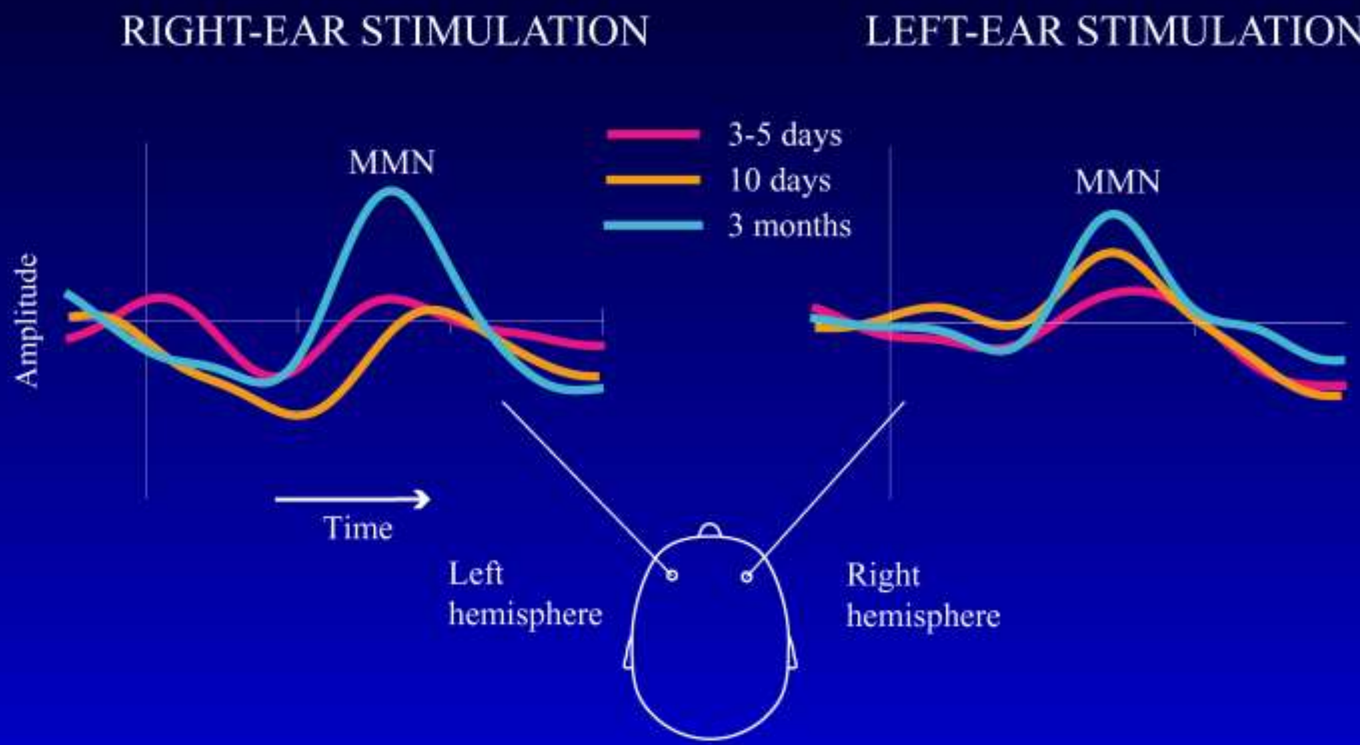
MMN to duration change was attenuated in children with Asperger´s syndrome, relative to that in controls, whereas that to frequency change and vowel change was unaffected (Lepistö *et al.*, in prep.).

MMN and P3a responses to a 10% frequency change in speech and non-speech sounds in autistic and control children



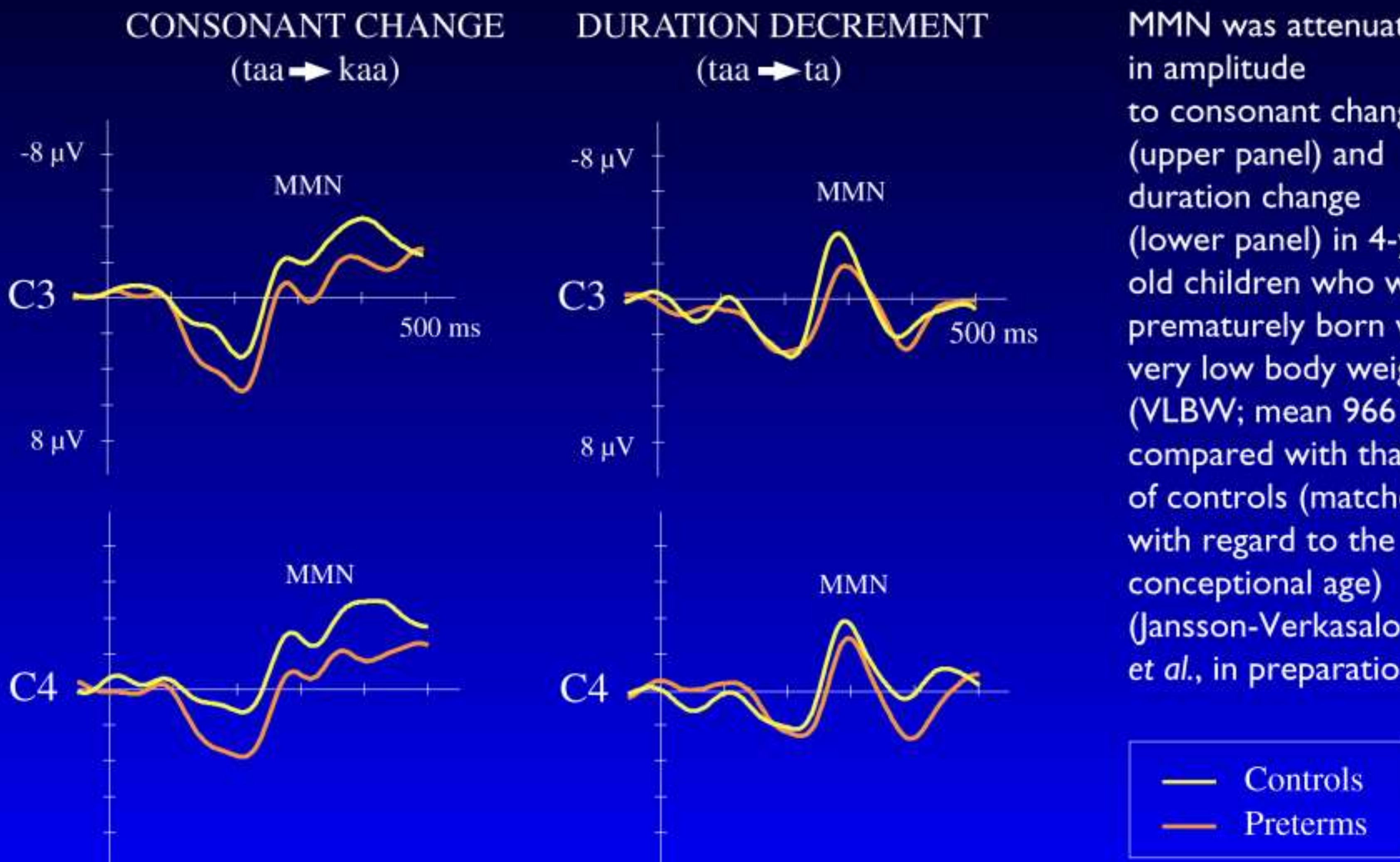
The frontal (F3) MMN and P3a responses evoked by 10% frequency change in speech and acoustically equal non-speech sounds in children with and without autistic syndrome (Čeponienė *et al.*, 2003).

MMN as an index of the recovery of frequency discrimination after a left-hemispheric stroke



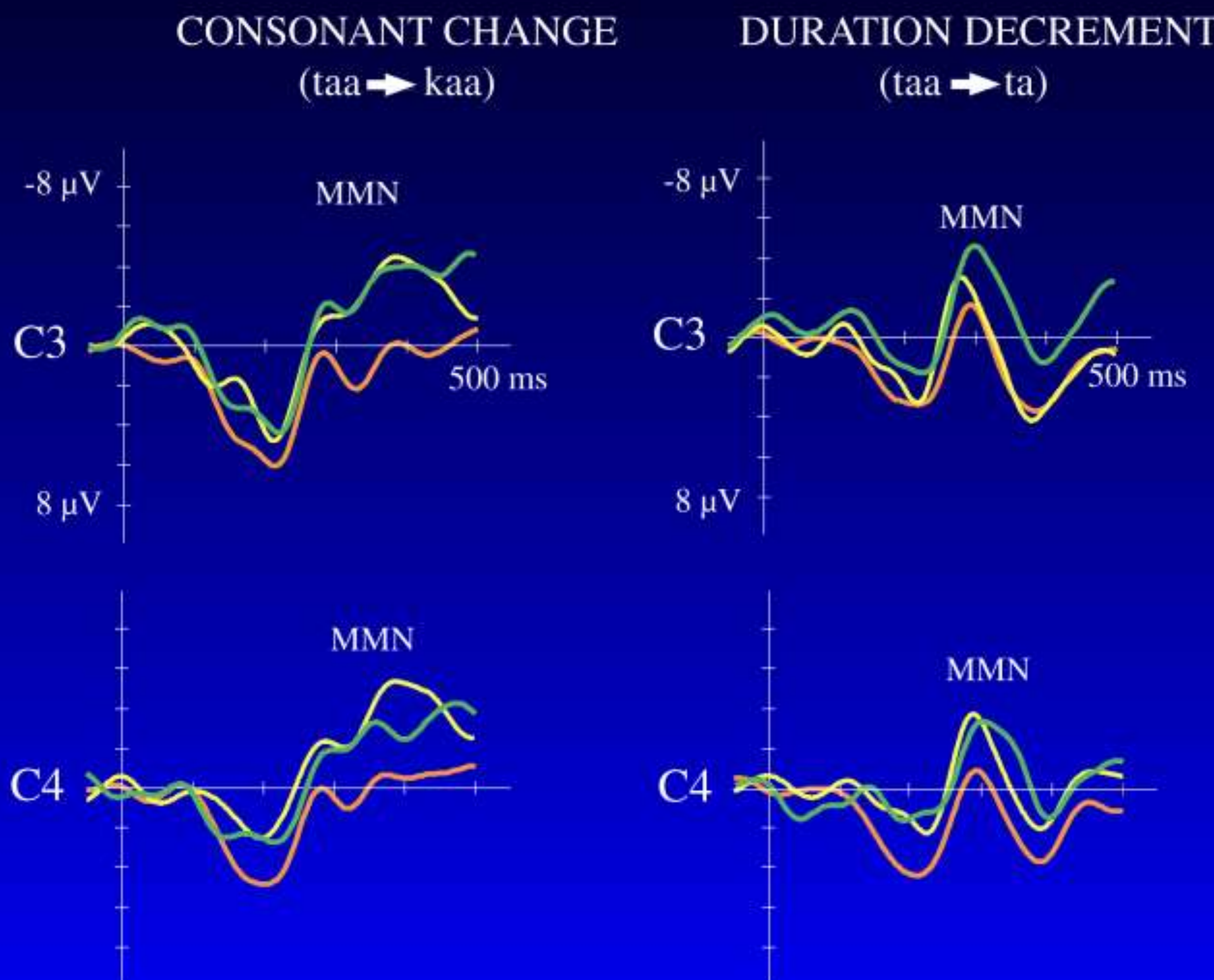
MMN shows how frequency discrimination recovered to normal levels within 3 months from the occurrence of a stroke (averaged data of 8 patients). This MMN recovery was slower with right-ear stimulation (with the main part of the auditory input going to the damaged left hemisphere) (curves on the left) than with left-ear stimulation (curves on the right) (Ilvonen *et al.*, submitted).

MMN shows deteriorated speech-sound processing in 4-yr old prematurely born VLBW children



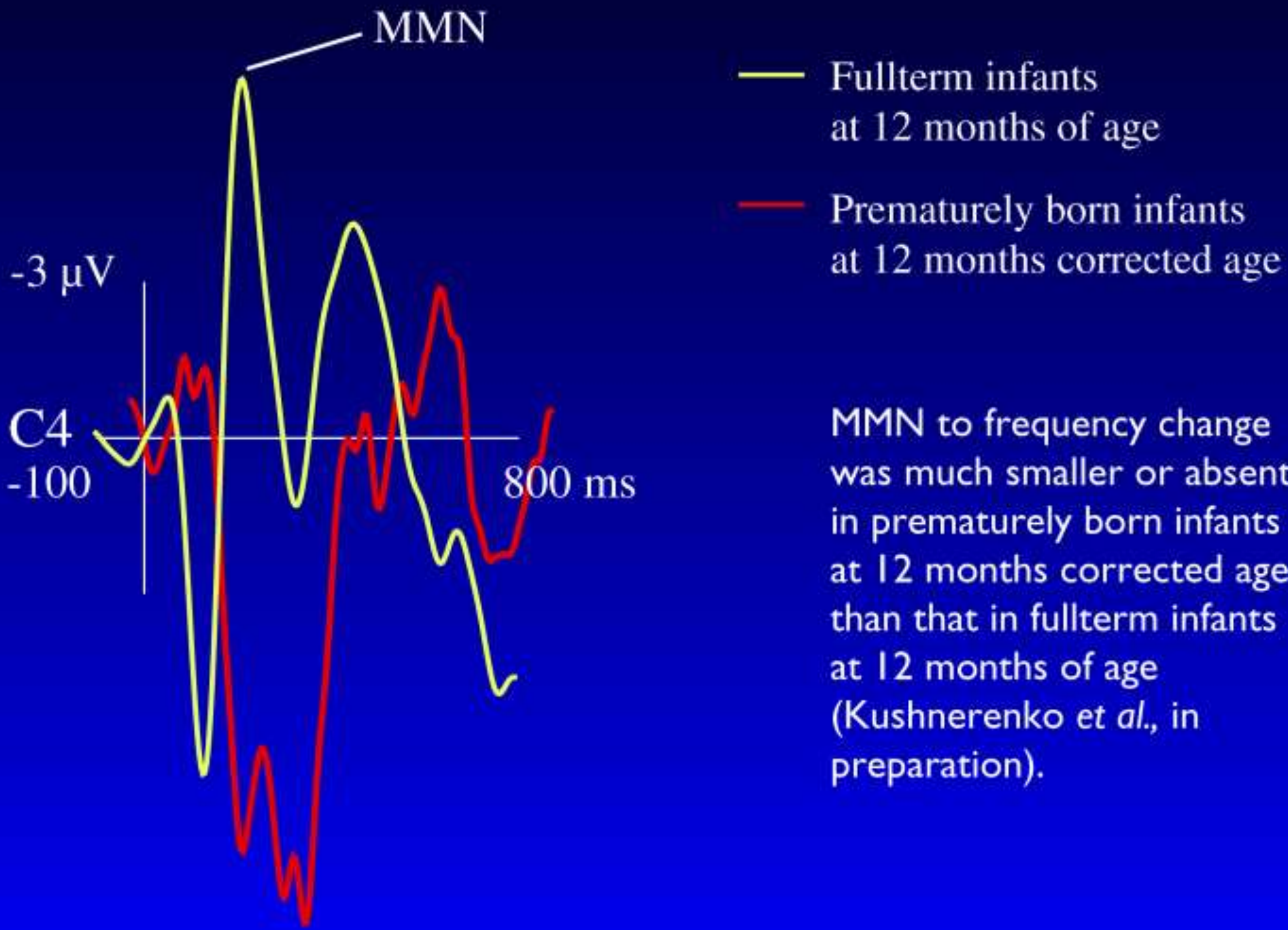
MMN was attenuated in amplitude to consonant change (upper panel) and duration change (lower panel) in 4-yr. old children who were prematurely born with very low body weight (VLBW; mean 966 g) compared with that of controls (matched with regard to the conceptional age) (Jansson-Verkasalo *et al.*, in preparation).

MMN shows deteriorated speech-sound processing in 4-yr old prematurely born VLBW children



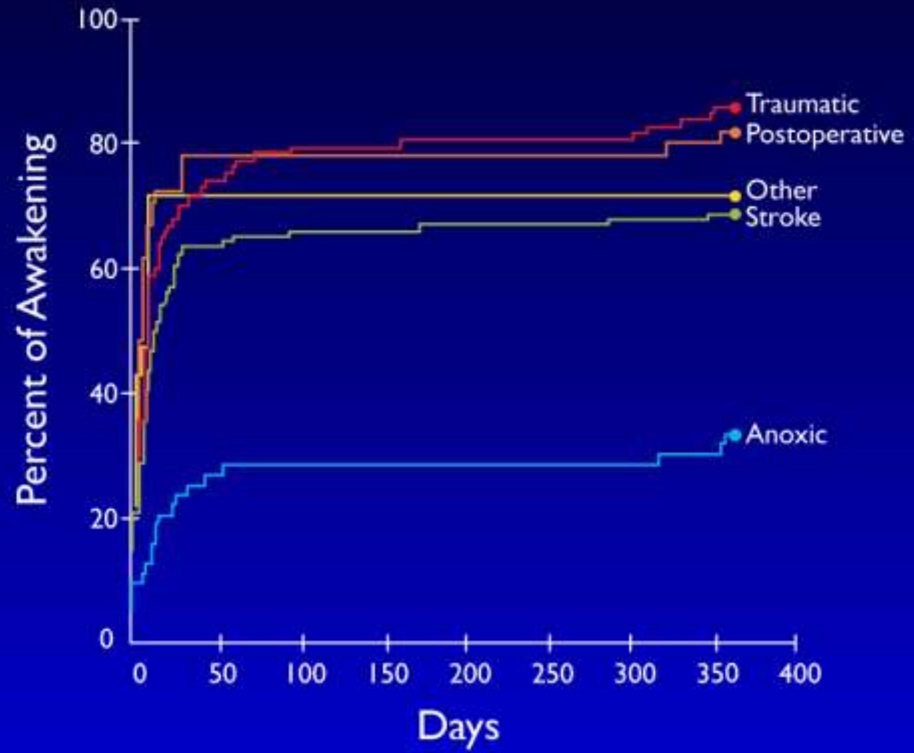
The MMN-amplitude attenuation presented in the preceding figure only involves those preterms who had naming difficulties, showing that the MMN -amplitude attenuation in prematurely born children indexes difficulties in language use (Jansson-Verkasalo et al., in preparation).

MMN shows auditory-processing abnormality in prematurely born infants at the age of 1 year



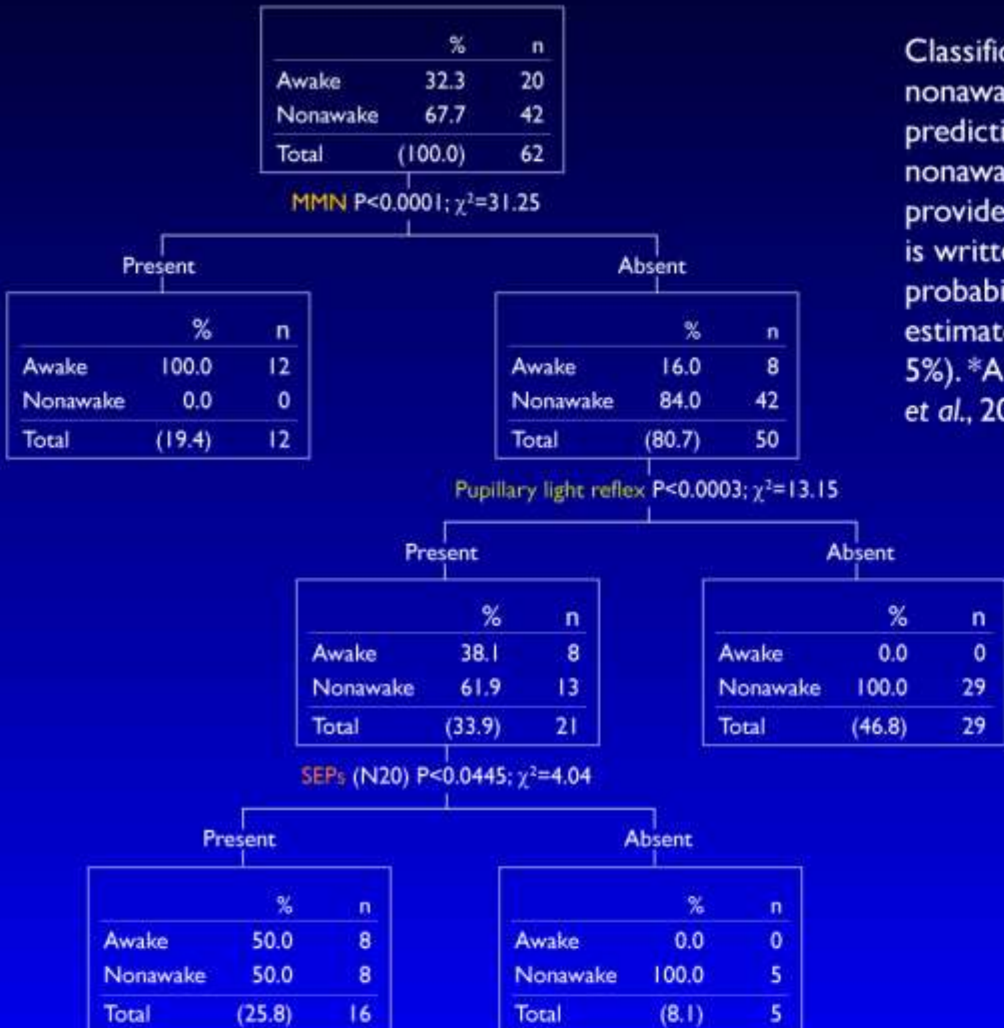
MMN to frequency change was much smaller or absent in prematurely born infants at 12 months corrected age than that in fullterm infants at 12 months of age (Kushnerenko *et al.*, in preparation).

Awakening curves as a function of time from coma with different etiologies



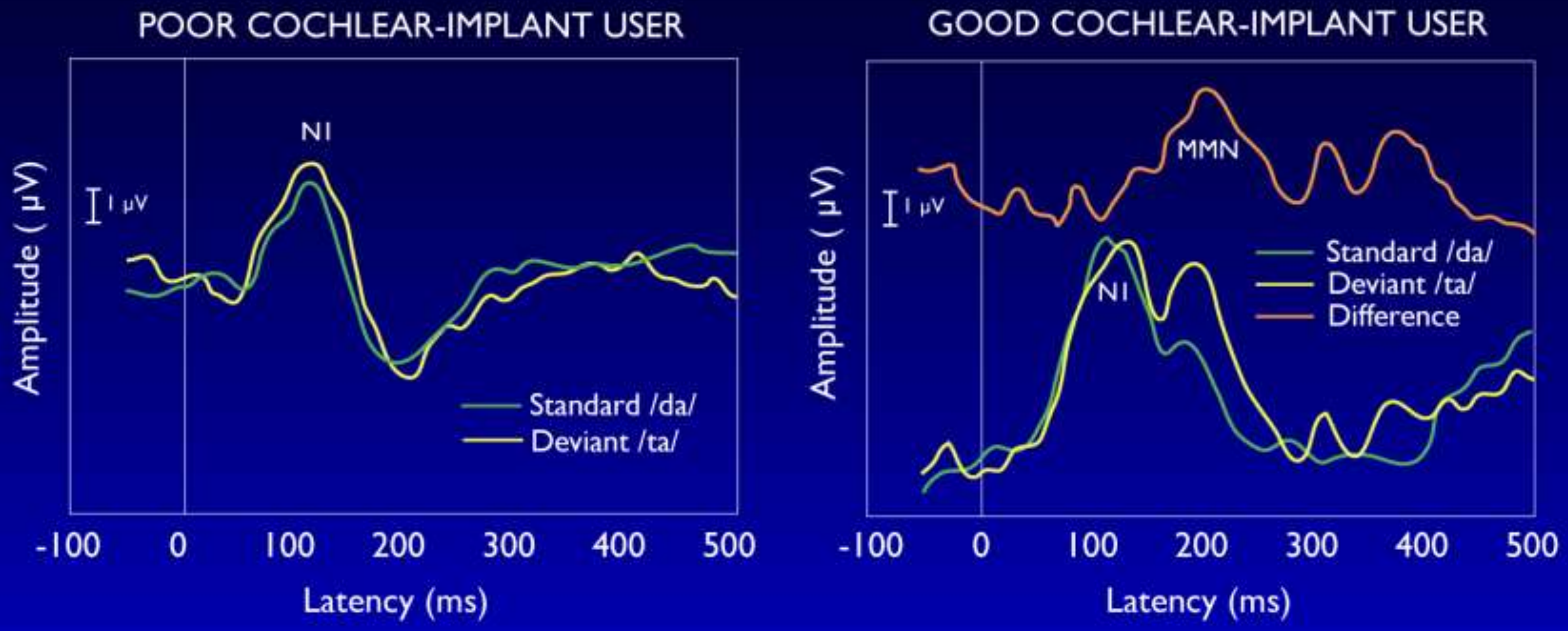
Kaplan-Meier survival curves for awakening according to etiologies. Etiologies from top to bottom: traumatic brain injury, postoperative, encephalitis (other), stroke, anoxic. Chi-square = 49.99, df = 4. Log-rank test, $p < 0.0001$ (Fischer *et al.*, 2004).

Classification tree analysis for awakening from severe anoxic coma



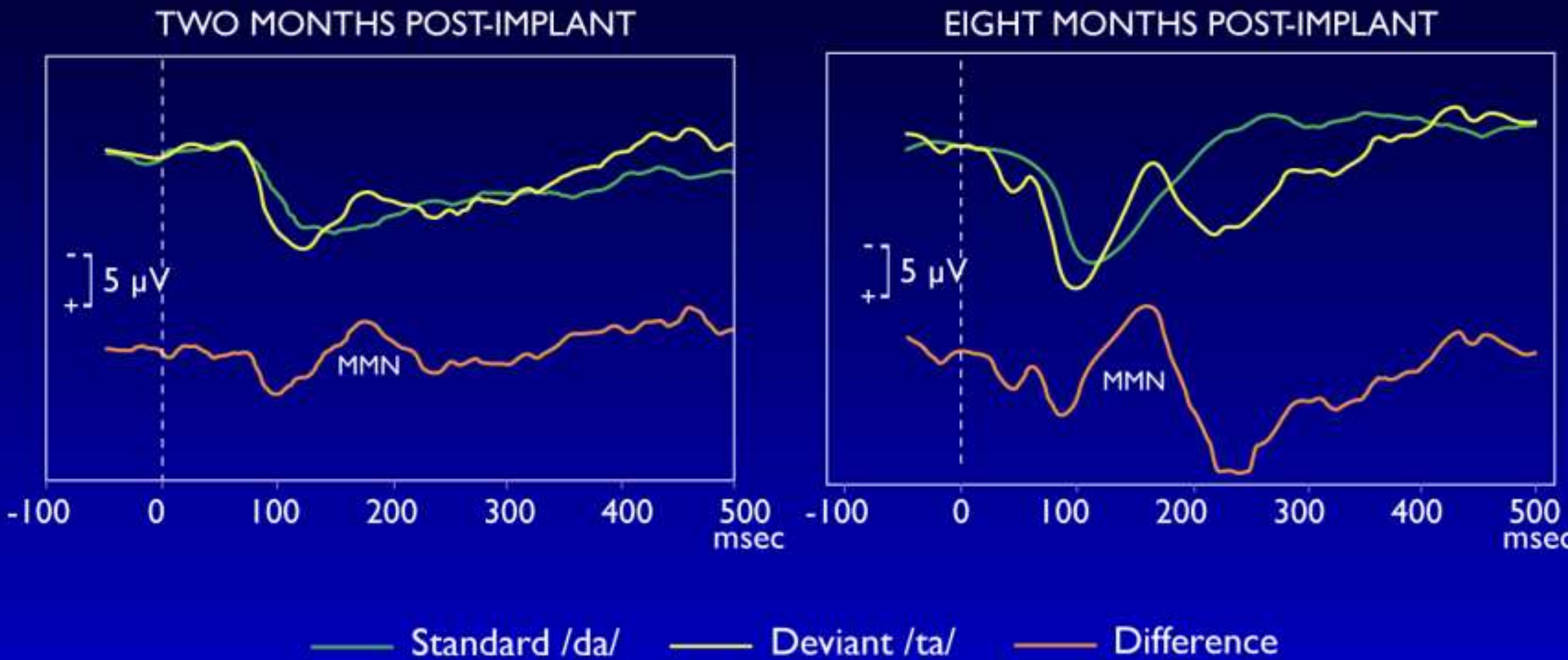
Classification tree analysis for awakening and nonawakening. This classification tree selects the best predictive variables to classify a patient as awake or nonawake at 12 months. The leaves of the tree provide a classification rule. The predicted category is written in bold in the corresonding box. The probability of misclassification using this rule was estimated by cross-validation at 19% (sensitivity = 5%). *All chi-square values are based on 1 *df* (Fischer *et al.*, 2006).

MMN indexes the success of cochlear-implant operation



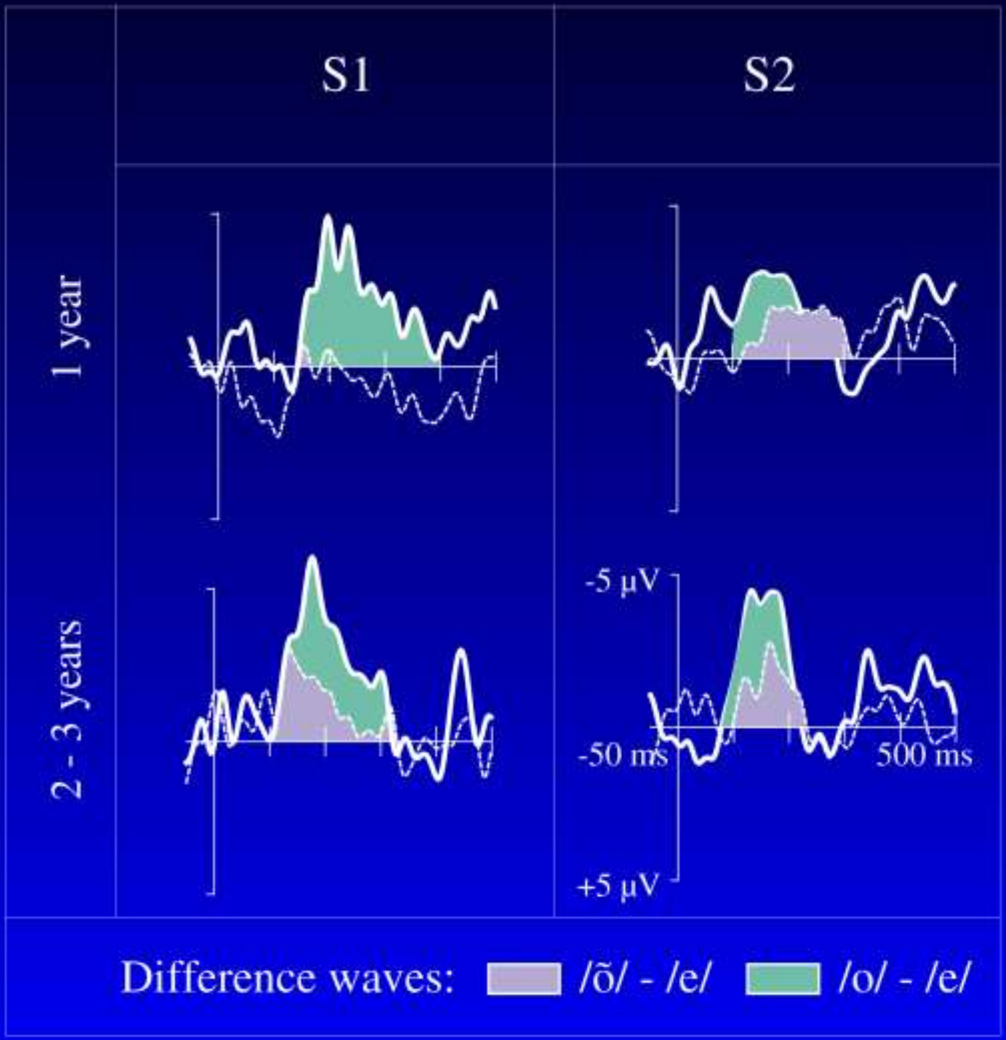
Left: ERPs to the standard stimulus /da/ and deviant stimulus /ta/ are very similar, there being no MMN in this cochlear-implant user. Consistent with this, the patient could discriminate speech sounds behaviourally only very poorly. *Right:* A clear MMN can be seen for this syllable contrast in this patient. Consistent with this, the patient could easily discriminate speech sounds behaviourally (Kraus *et al.*, 1993).

MMN indexes the improvement of vowel discrimination as a function of time since cochlear-implant installation



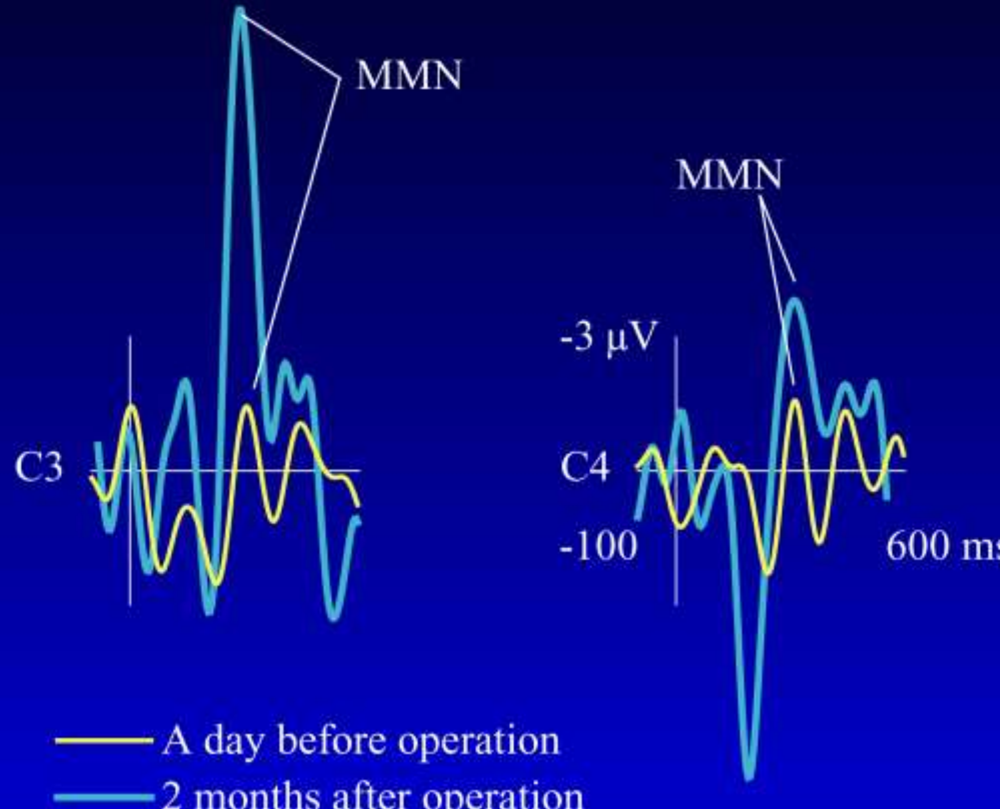
MMN of a cochlear-implant patient was small in amplitude 2 months` post-implant (left) but was considerably enhanced at 8 months post-implant (right). Consistent with this, his behavioural speech-sound discrimination ability was much better at 8 than at 2 moths post-implant (Kraus & McGee, 1993).

MMN shows long-term improvement of wovel discrimination in cochlear-implant users



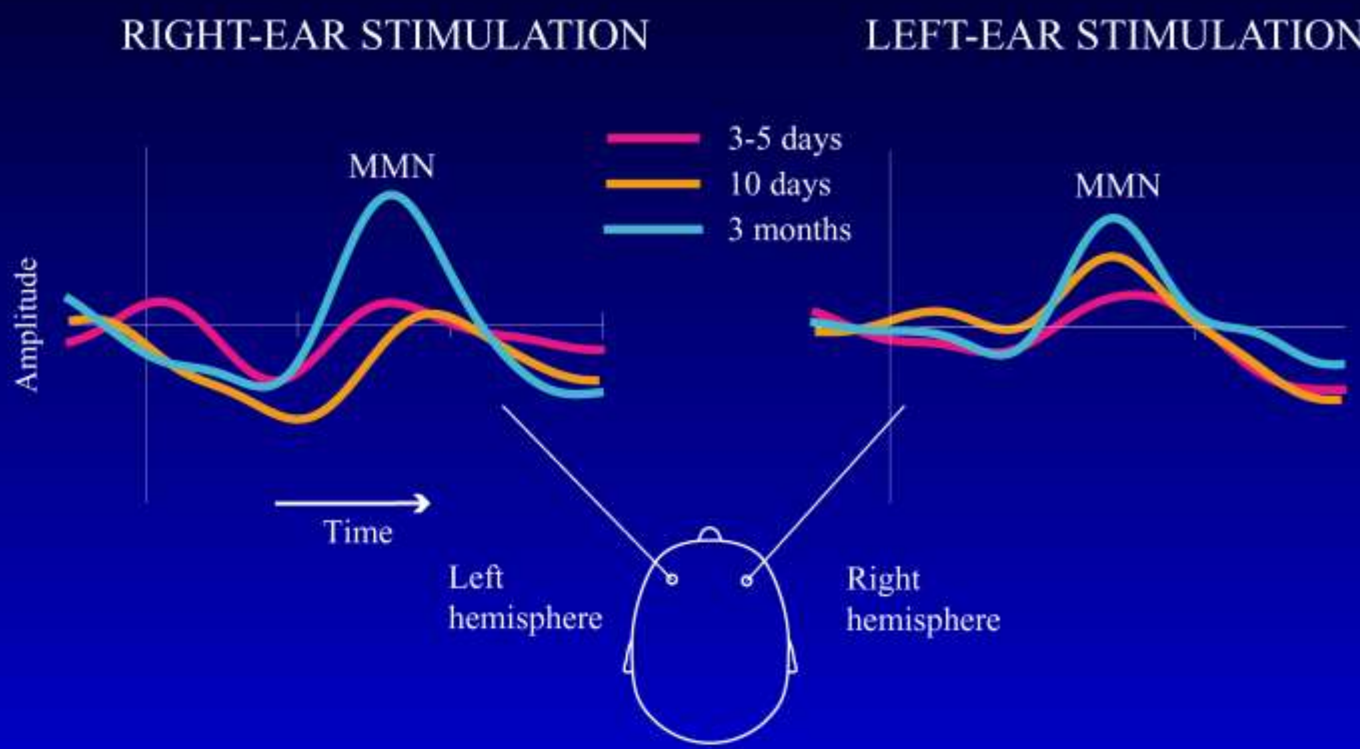
MMN as a function of time since cochlear-implant installation in two individual patients (S1, S2) for an acoustically larger (/o/-/e/; green) and smaller (/õ/-/e/; grey) phoneme change. MMN peaks earlier and gets larger in amplitude between 1 year and 2-3 years from implant installation (Lonka *et al.*, in press).

MMN indicates the improvement of central auditory processing in microcephalic infant after cranioplasty



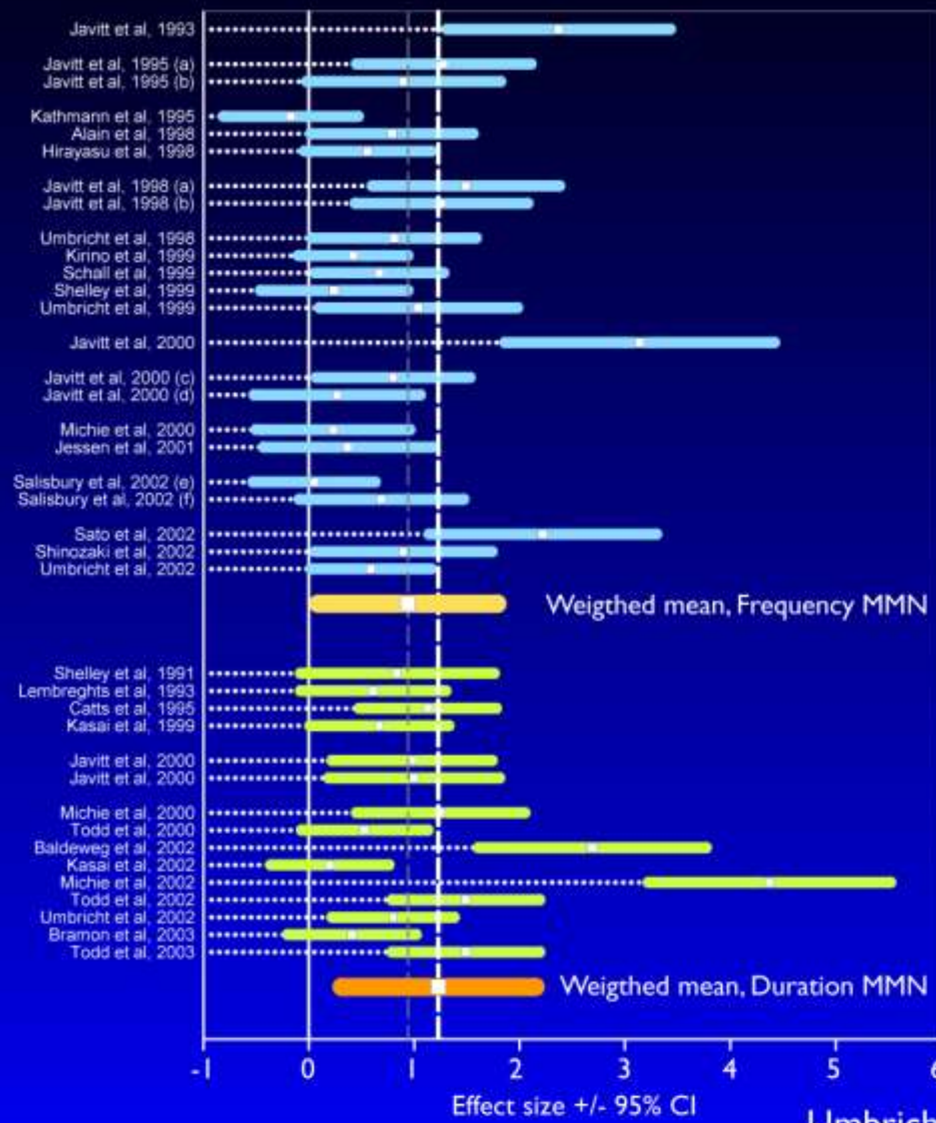
Before the scull operation of a microcephalic infant, no MMN was elicited by a sound-frequency change, whereas 2 months after the operation, an MMN of large size was elicited by the same sound change, indexing a considerable improvement of central auditory processing as a result of the operation (Kushnerenko *et al.*, in preparation).

MMN as an index of the recovery of frequency discrimination after a left-hemispheric stroke



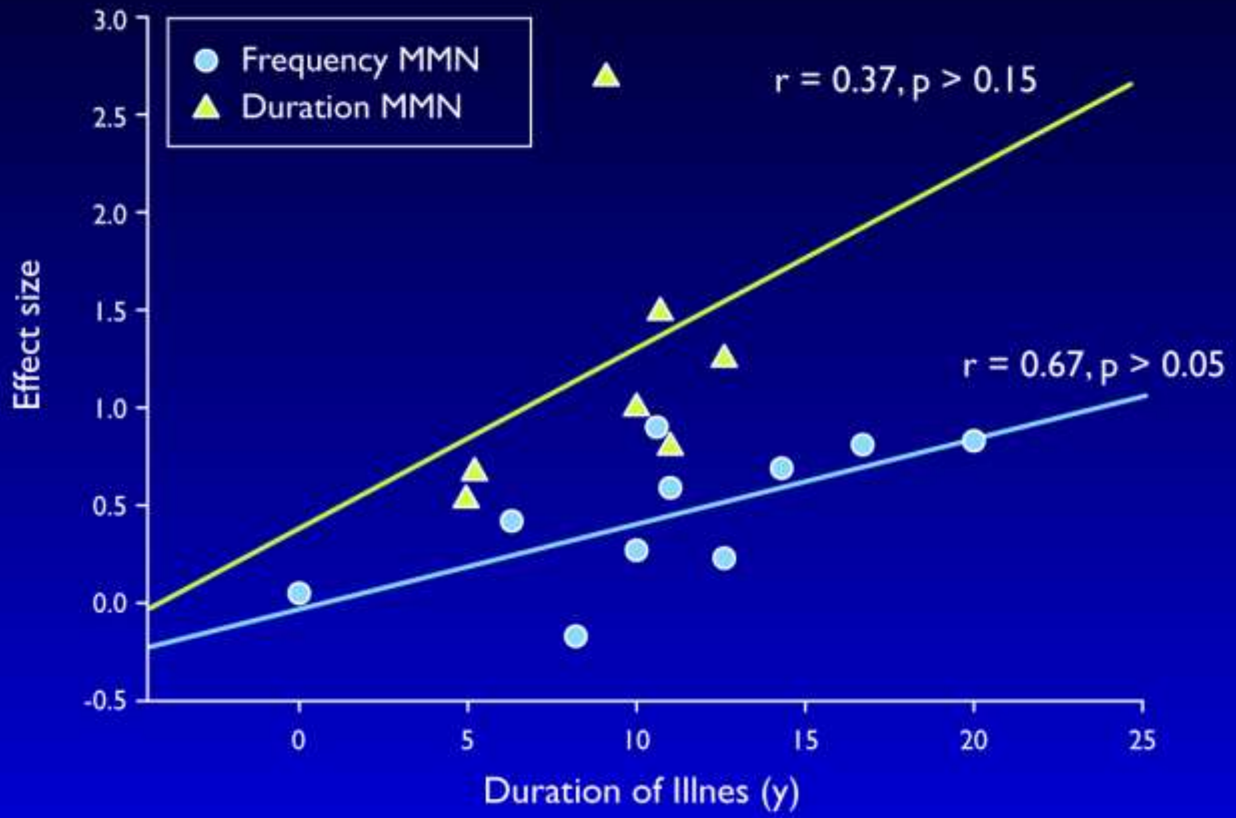
MMN shows how frequency discrimination recovered to normal levels within 3 months from the occurrence of a stroke (averaged data of 8 patients). This MMN recovery was slower with right-ear stimulation (with the main part of the auditory input going to the damaged left hemisphere) (curves on the left) than with left-ear stimulation (curves on the right) (Ilvonen *et al.*, submitted).

Meta-analysis: MMN in schizophrenia



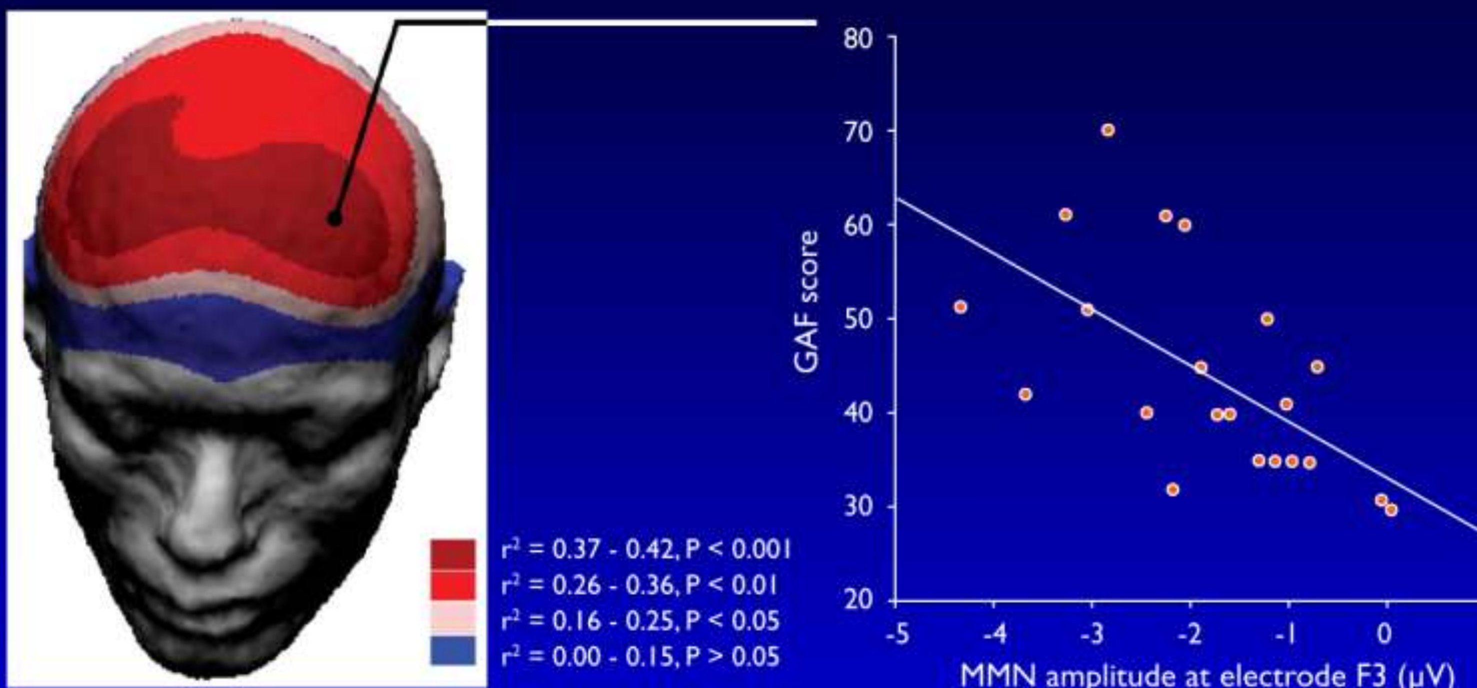
Umbricht *et al.*, in press

MMN in schizophrenia



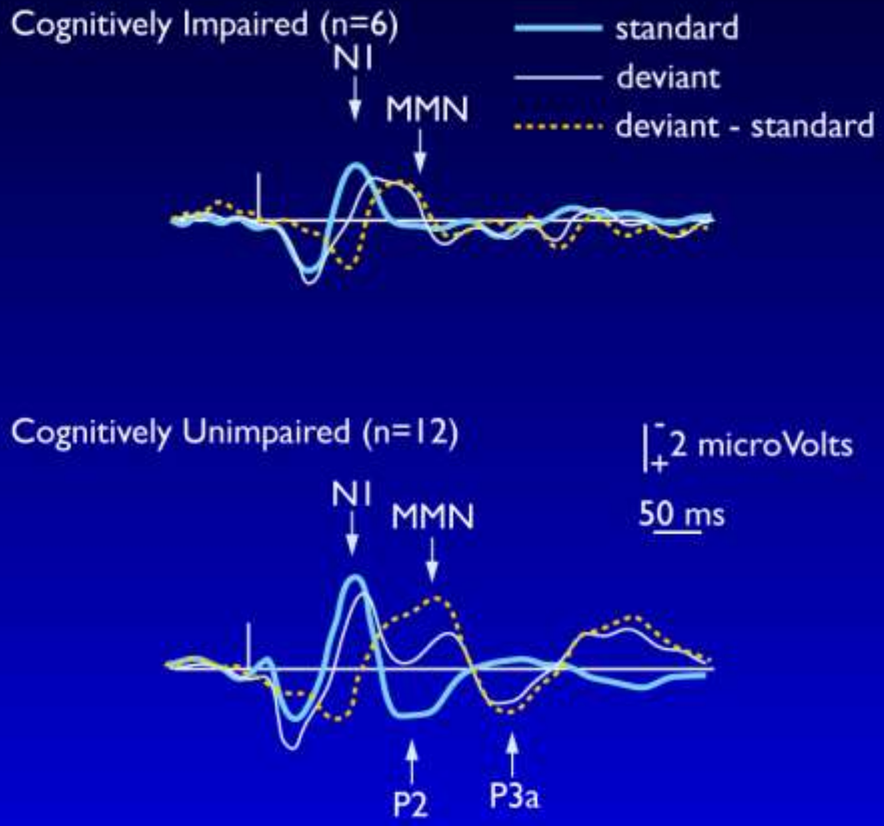
Umbricht *et al.*, in press

MMN in schizophrenia



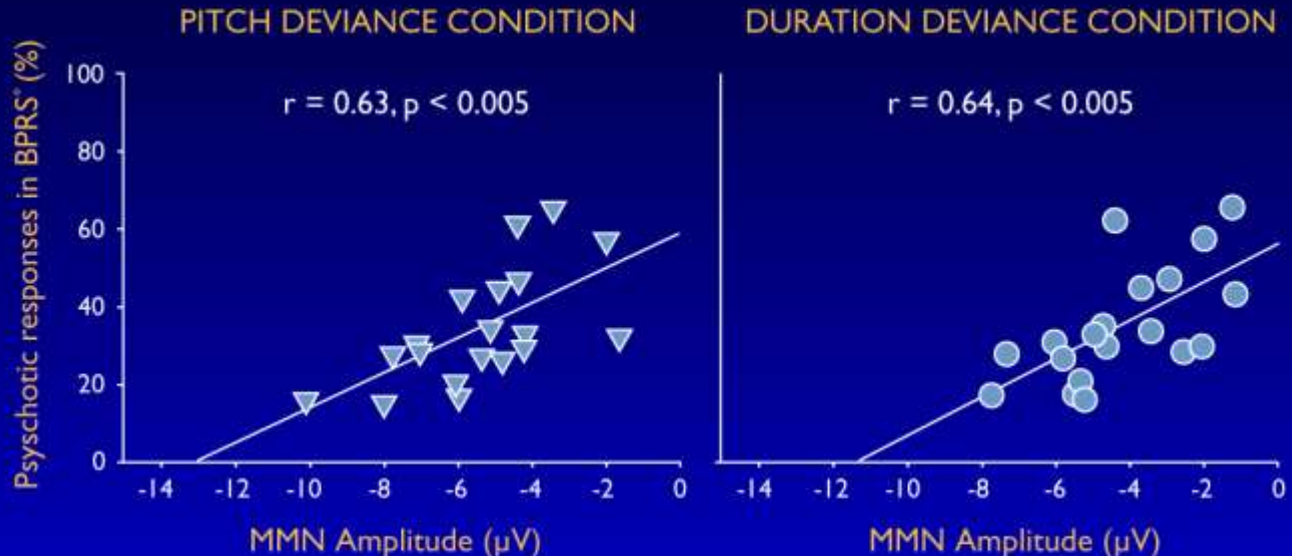
Light *et al.*, 2005

MMN reflects cognitive impairment in MS



Grand-average waveforms elicited by the auditory oddball passive task across the 6 patients with a global cognitive impairment (top) and averaged across the 12 patients without cognitive impairment (bottom). Thick line: responses to standard sounds, thin line: responses to deviant sounds, dashed line: difference deviant minus standard. ERPSs were averaged in patients showing a significant MMN only. Stimulus position: vertical bar. Data were filtered 3-30 Hz (Jung *et al.*, 2006).

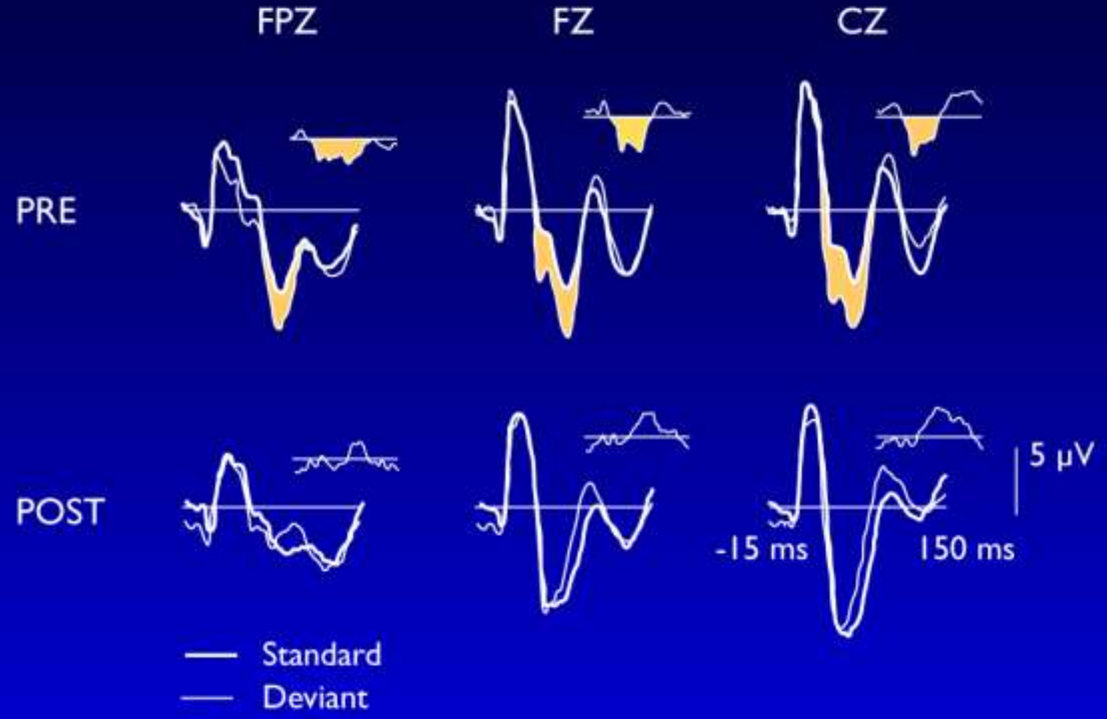
MMN as an index of the functional condition of the NMDA-receptor system



*Brief Psychiatric Rating Scale (BPRS)

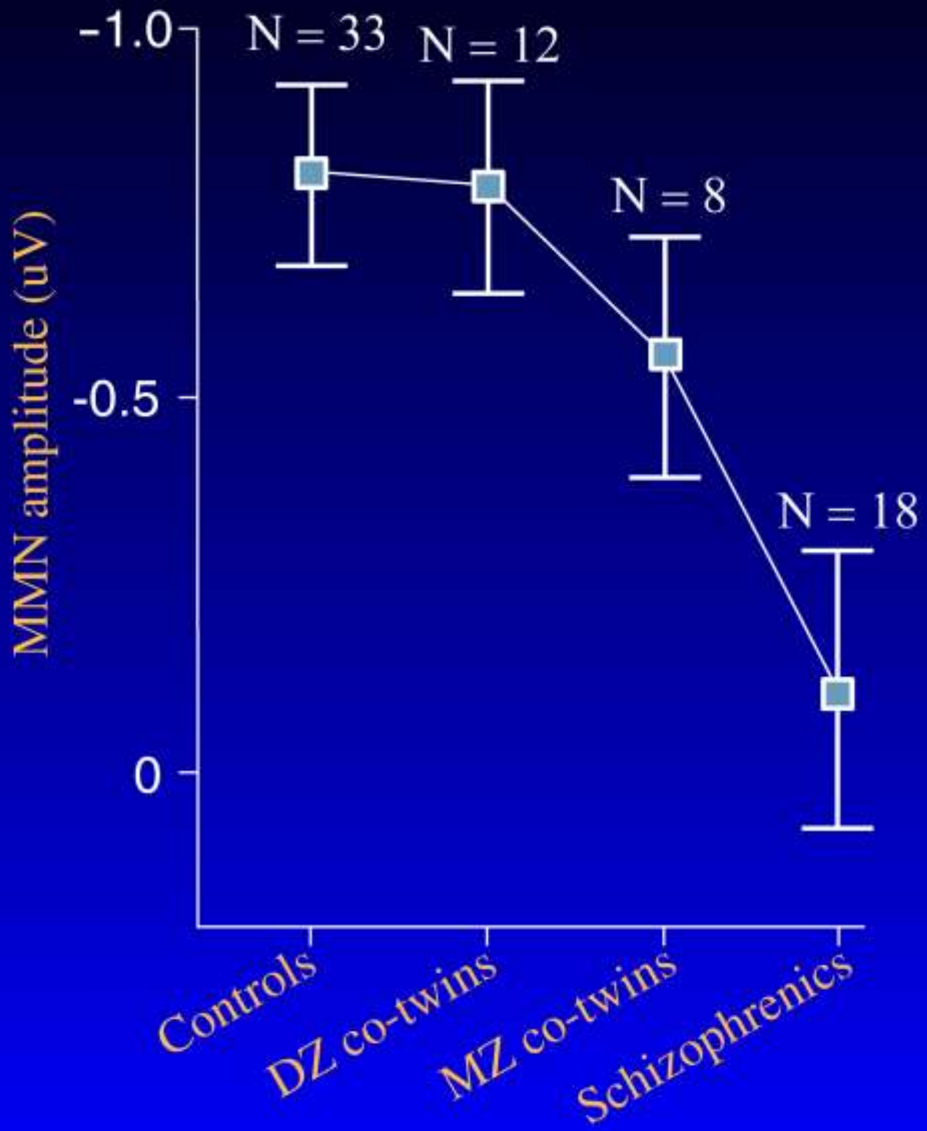
Umbricht *et al.*, 2001

Epidural waveforms pre- and post-MK801 administration



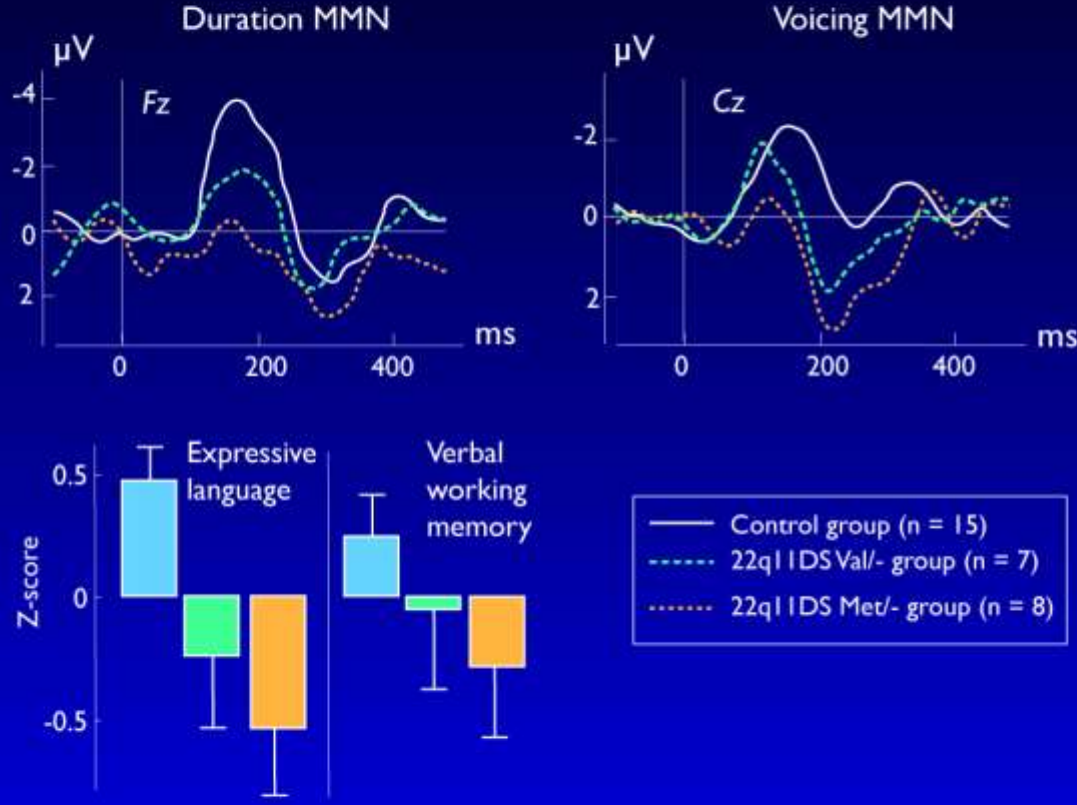
Javitt *et al.*, unpublished data

MMN suggests genetic disposition to schizophrenia



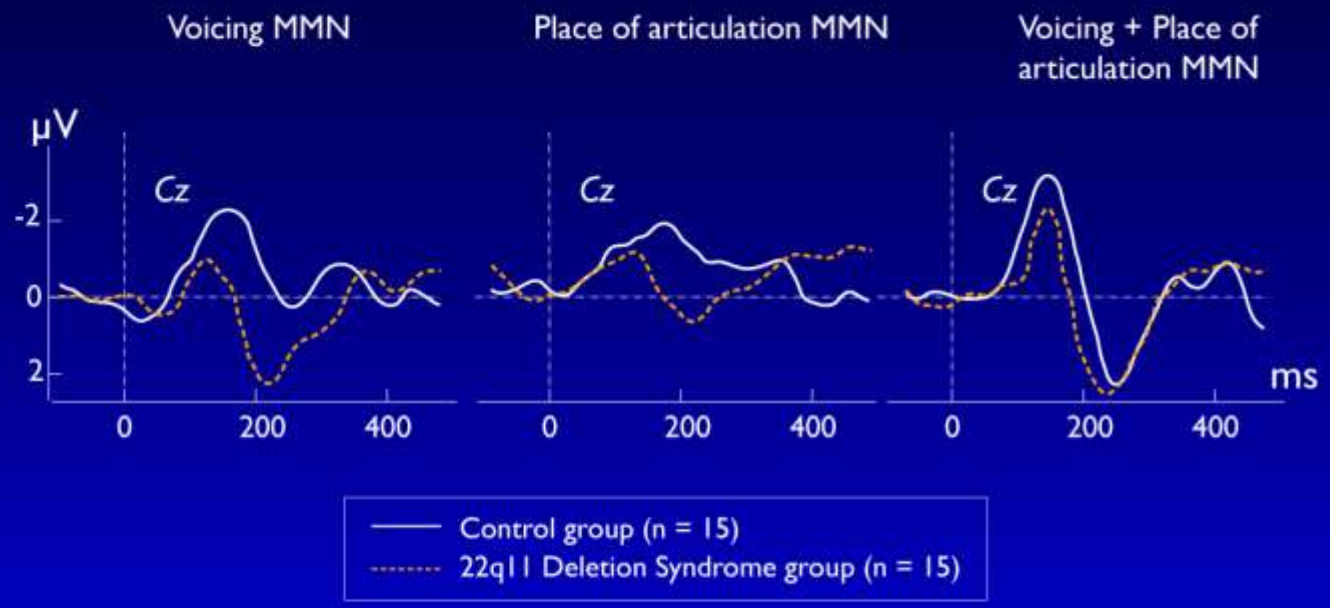
The MMN amplitude for frequency change of monozygotic (MZ) co-twins of schizophrenic patients was attenuated in amplitude, whereas that of dizygotic (DZ) co-twins was not, in relation to the MMN amplitude of controls, showing that MMN indexes genetic disposition to schizophrenia. During the MMN measurements, subjects were watching video-films (Ahveninen *et al.*, in preparation).

MMN and language/memory performance in 22q11 Deletion Syndrome: modification of endophenotypes by *COMT* Val108/158Met polymorphism



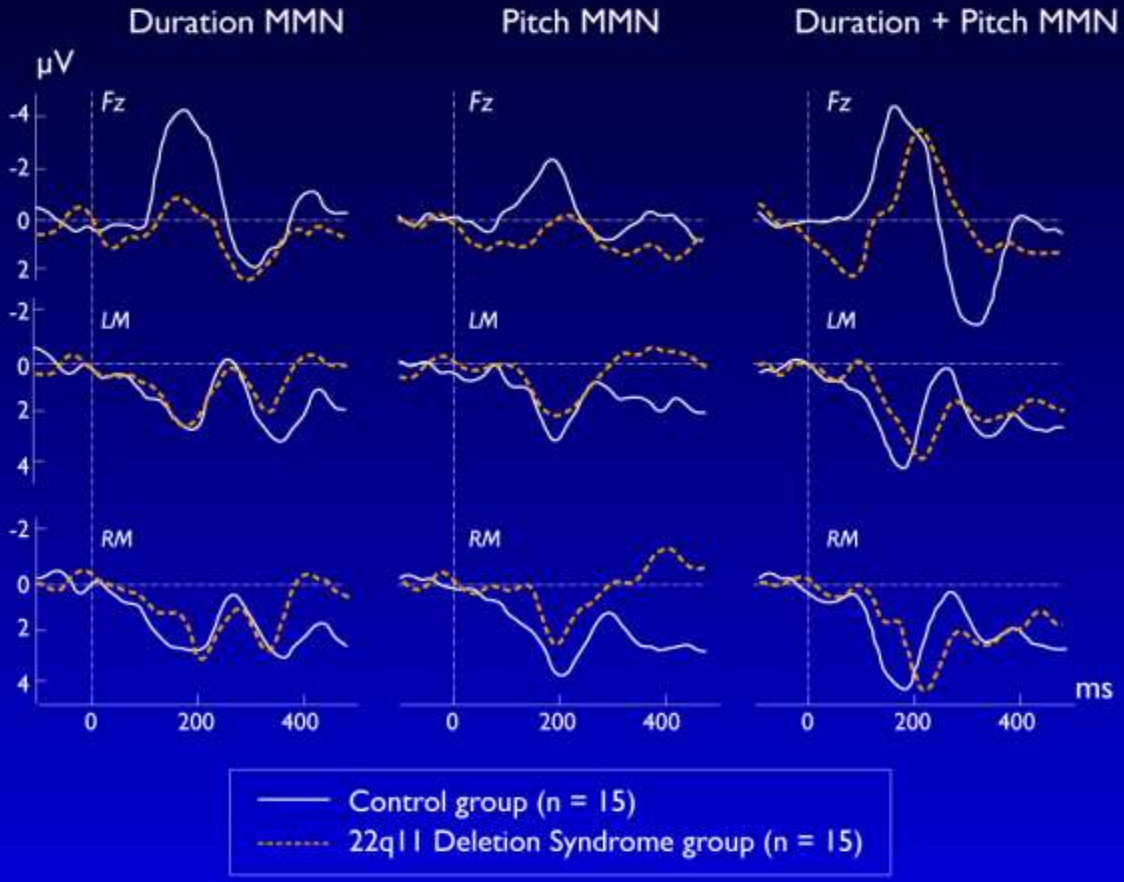
Baker *et al.*, 2005

MMN in 22q11 Deletion Syndrome



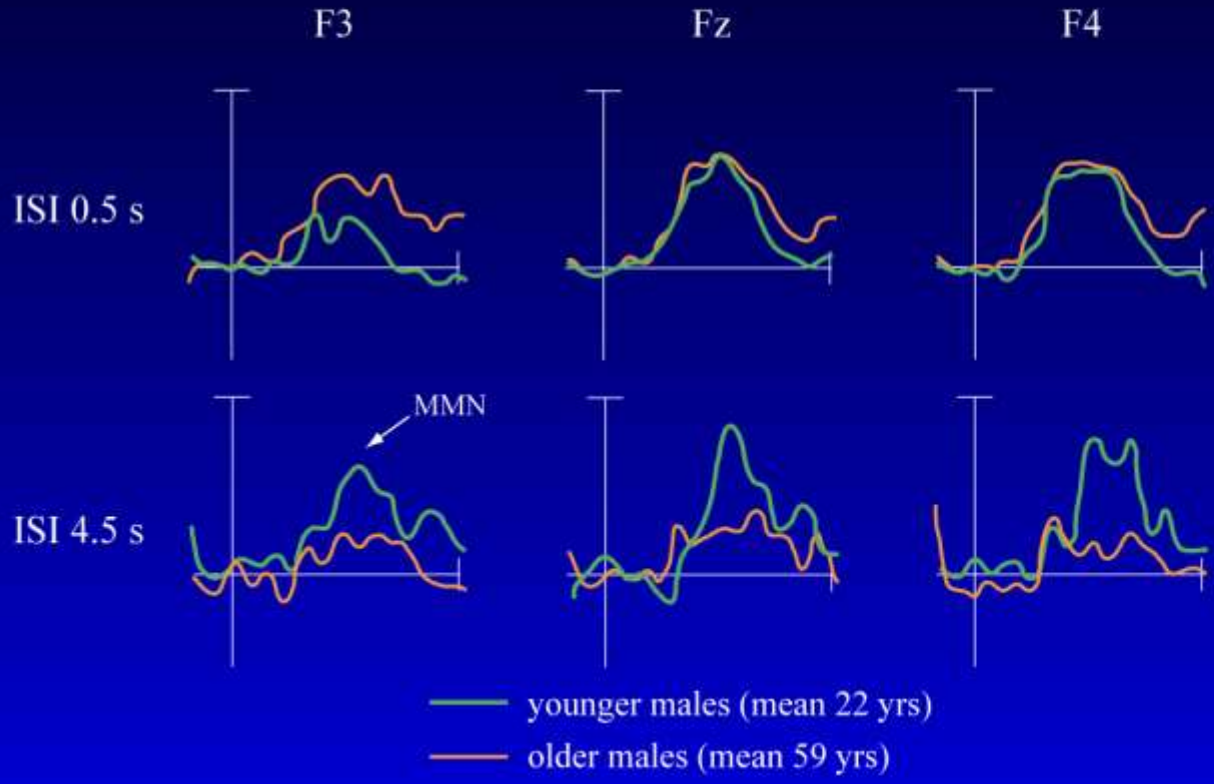
Baker *et al.*, 2005

MMN in 22q11 Deletion Syndrome



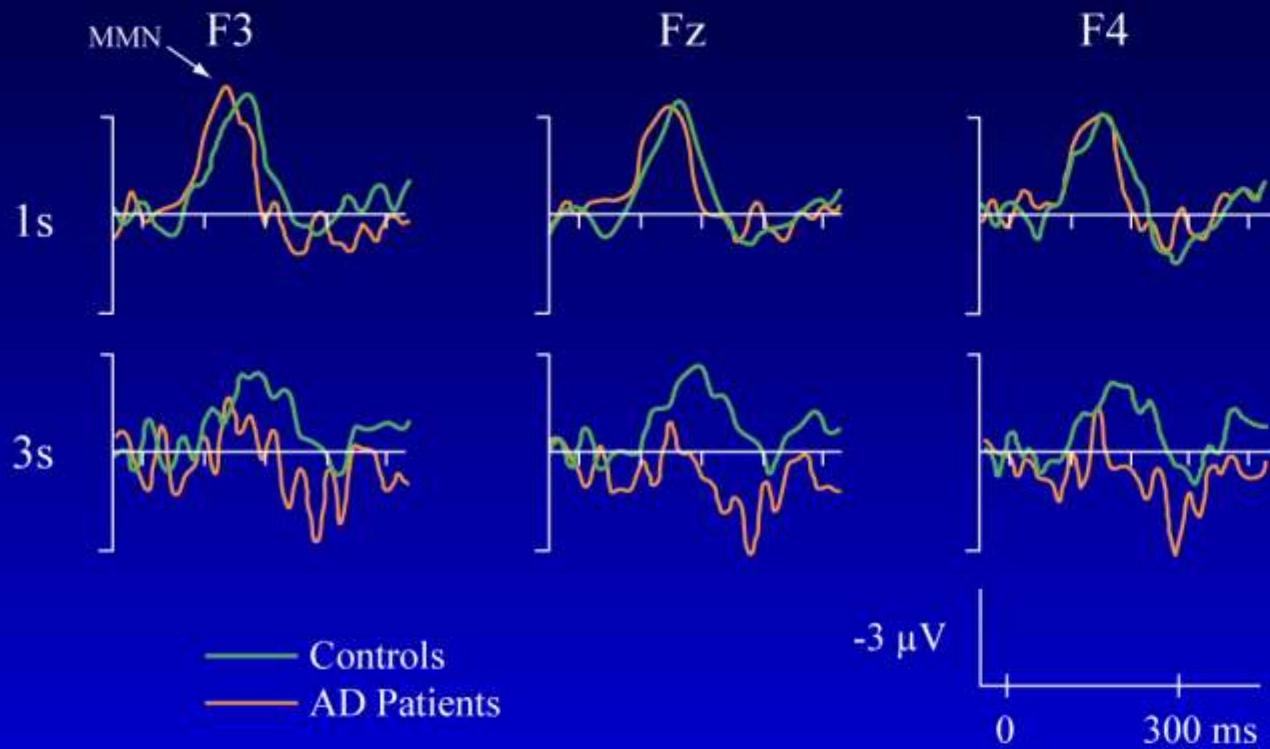
Baker *et al.*, 2005

MMN to frequency change indexes normal auditory discrimination but shortened sensory-memory duration with aging



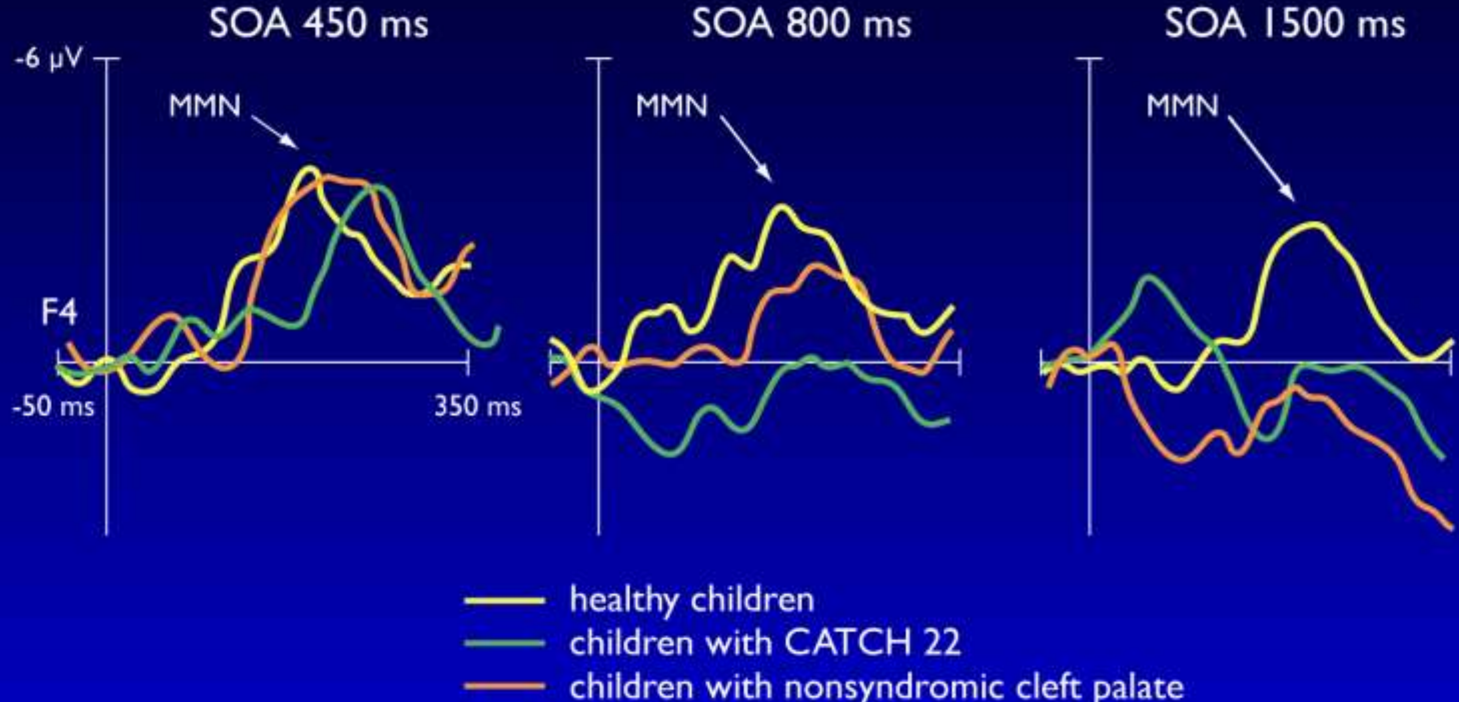
MMN to frequency change (700 → 600 Hz) was normal in older males with an ISI (inter-stimulus interval) of 0.5 sec but was considerably attenuated, relative to that of younger males, with an ISI of 4.5 sec, indexing faster auditory sensory-memory trace decay, and thus decreased brain plasticity with aging (Pekkonen *et al.*,1996).

MMN to frequency change shows normal auditory discrimination but shortened sensory memory duration in AD patients



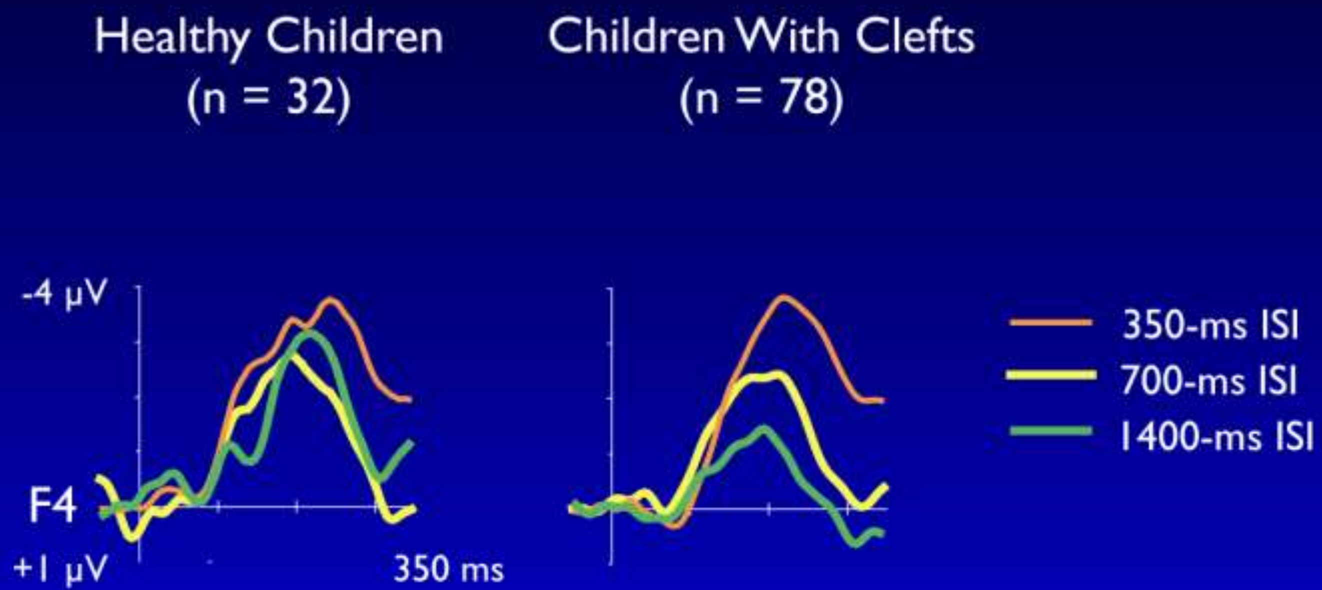
MMN to frequency change was normal in Alzheimer's patients with a 1-sec inter-stimulus interval (ISI), suggesting normal auditory perception, but was considerably smaller than that of controls with a 3-sec ISI, indexing faster auditory sensory-memory trace decay, and thus decreased brain plasticity in these patients (Pekkonen et al.,1994).

MMN shows shortened duration of auditory sensory memory in children with CATCH 22 and with nonsyndromic cleft palate



MMN was of normal amplitude in children with CATCH 22 and in children with nonsyndromic cleft palate when the SOA (stimulus-onset-asynchrony) was short (450 ms) but was considerably attenuated, relative to that of controls, or totally absent when the SOA was prolonged to 800 ms and 1500 ms, suggesting abnormally rapid sensory-memory decay in these patient groups (Cheour *et al.*, 1998).

MMN shows shortened sensory-memory duration in children (7-9 years) with oral clefts



MMN was of normal amplitude in 7-9 years old children with oral clefts when a short ISI (350 msec) was used but was considerably smaller than that of controls when the ISI was prolonged to 700 ms and to 1400 ms, suggesting an accelerated sensory-memory trace decay in the patients (Ceponiene *et al.*, 1999).

MMN in clinical research and praxis

I MMN PROVIDES AN OBJECTIVE INDEX OF

A) central auditory-processing deterioration / abnormality in
- e.g. Asperger´s syndrome, autism, cochlear-implant users, dyslexia, schizophrenia

B) central auditory-processing improvement in
- e.g. children operated for craniosynosthosis, dyslexic children receiving remediation training

C) illness progression in
- e.g. schizophrenia

D) shortened auditory sensory-memory duration (=decreased brain plasticity) in
- e.g. alzheimer's patients, children with cleft palate, chronic alcoholism, normal aging

E) general brain degeneration in
- e.g. patients with diabetes mellitus, Alzheimer's disease, HIV, Parkinson´s disease, schizophrenia

F) drug effects on central auditory processing
- e.g. alcohol, antihistamine, clozapine, haloperidol, ketamine, naltrexone, oxytocin, vasopressin

G) decreased automatic attention switching in
- e.g. alcohol-intoxicated persons, schizophrenic patients

H) increased automatic attention switching (increased distractibility) in
- e.g. closed head injury (even in the absence of visible MRI abnormalities)

I) genetic risk of
- e.g. dyslexia, schizophrenia

J) functional state of
- eg. the central nervous system in fetus and early infancy, the NMDA-receptor system

MMN in clinical research and praxis

II MMN PREDICTS THE RECOVERY FROM

A) coma
B) craniosynosthosis after scull operation
C) neglect (hemifield inattention)

III MMN CAN BE USED TO ON-LINE MONITOR

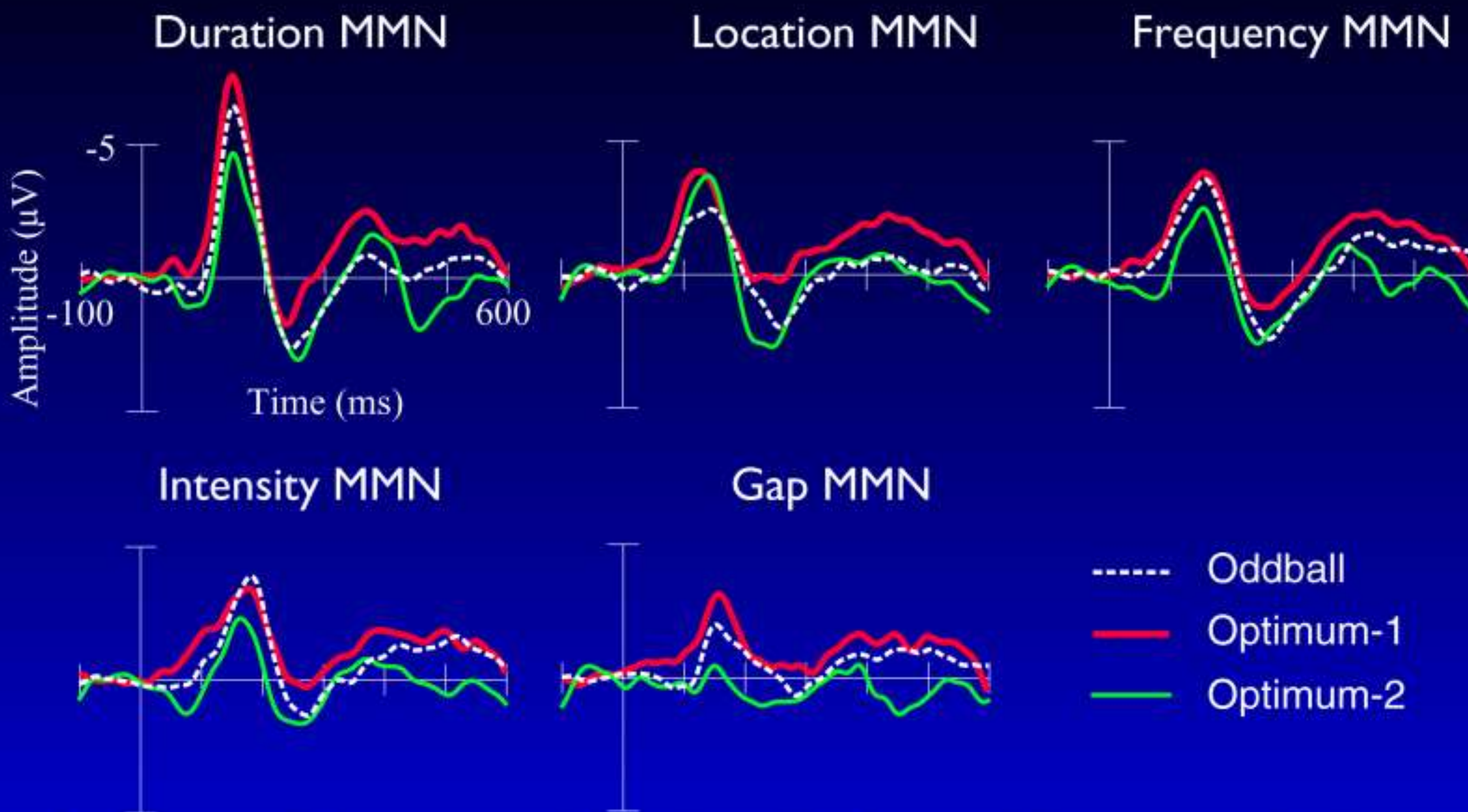
A) coma state

IV MMN INDEXES THE OCCURRENCE OF SOUND DISCRIMINATION IN

A) anaesthesis
B) apallic patients with severe traumatic and non-traumatic injuries
C) coma
D) fetuses
E) hypnosis
F) locked-in state
G) neglect and auditory extinction
H) newborns
I) prematurely born infants

Towards the optimal MMN paradigm

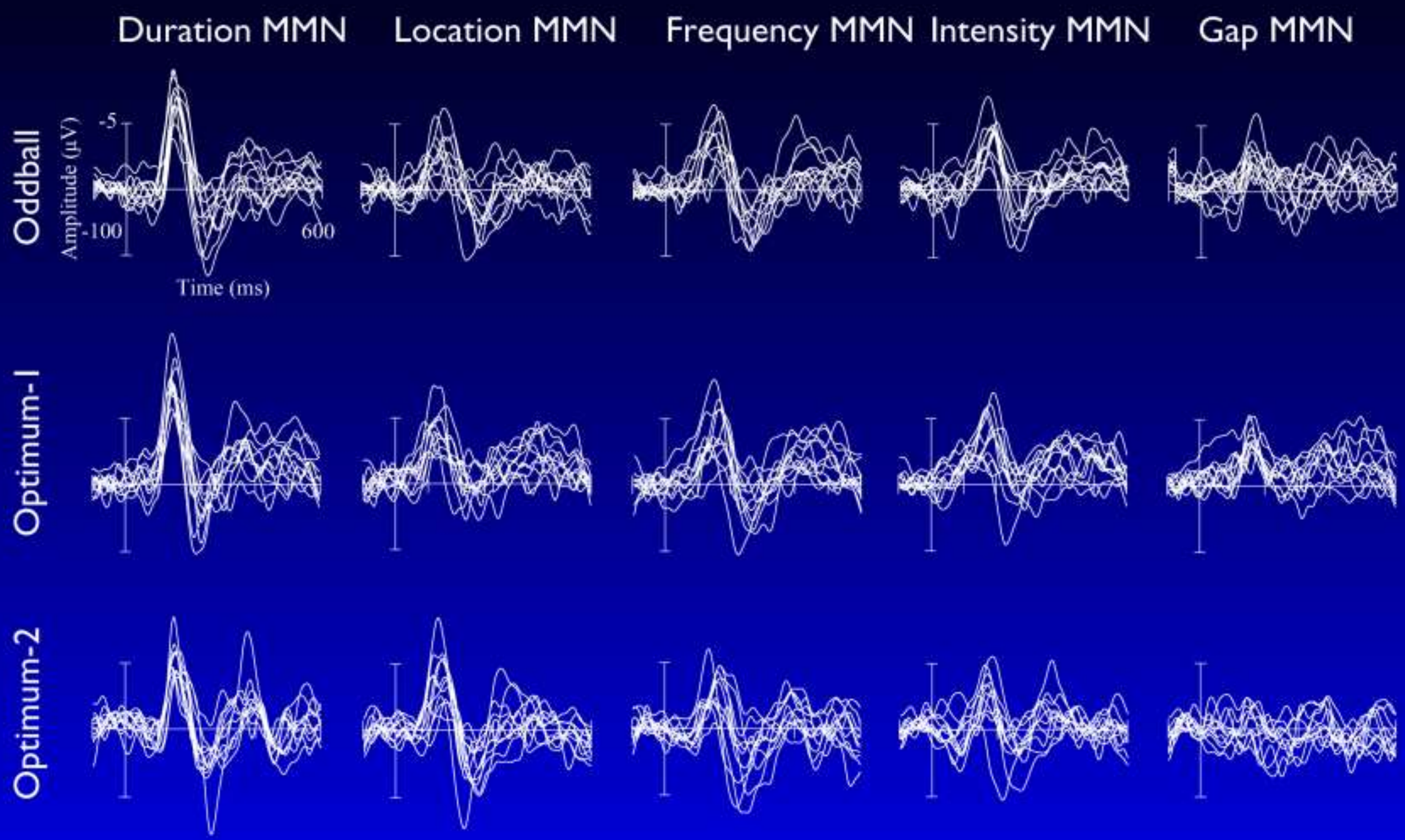
Grand-average difference waves



Grand-average difference waves (11 subjects) for 5 types of deviations recorded at a frontocentral electrode (approximately Fcz). Overlayed are the MMNs for the same type of deviation in the different conditions. The dotted line indicates the MMN in the traditional Oddball condition, the red line that in Optimum-1 condition, and the green line that in Optimum-2 condition. (Näätänen *at al.*, in press).

Towards the optimal MMN paradigm

Individual subtraction waves



Difference waves (11 subjects) for 5 types of deviations recorded at a frontocentral electrode (approximately Fcz). Plotted in columns are the 5 MMN types and in rows the conditions Oddball, Optimum-1 and Optimum-2. (Näätänen *et al.*, in press).

MMN research 2005

Europe

World