**Discriminative**

**Cortical Auditory Potentials**

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**Cortical Auditory Potentials**

- **Obligatory**
  - N1-P2 Complex

- **Discriminative**
  - Attending
    - N2-P3 Complex
  - Non-Attending
    - MMN

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**Diagrams**

- N1-P2 Complex
- N2-P3 Complex
- MMN
EEG (Electroencephalogram)

EEG can be recorded from multiple sensors on the scalp.
International 10-20 electrode system

Appropriate locations of electrodes can measure both poles of dipole
Vertical Dipole

There are only 2 ways a dipole source can be localized by EEG

- Highest amplitude on a referential (monopolar) recording
- Phase reversal on a bipolar recording

Advantages of EEG

- Best spatio-temporal resolution
  - Temporal resolution: 1 msec (1000 Hz) or better
  - Spatial resolution: 10 microns

- Can measure while behavioral activities are on-going
ERP (Event Related Potentials)

- Electrodes on scalp record voltage on many trials
- Average waveforms (aligned) "average out" the activity unrelated to that stimulus or response onset
- Average waveform: +ve and -ve peaks associated with particular processes

Averaging ERPs: Basic Idea
Where do potentials come from?

- Not action potentials…
- EPSPs & IPSPs most likely source

What do they mean?
Processing of sensory stimulus features is essential for humans determining their responses and actions.

Consequently, it is important to understand the brain mechanisms of sensory information processing, that is, "The Sensory Prerequisites of Cognition"
**History**

- Hans Berger 1929
- Pauline Davis 1939
- Hallowell Davis 1964
- Samuel Sutton 1965
- Risto Näätänen 1978

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**Discriminative Cortical Auditory Potentials**

**Technical Aspects**
- Stimulation technique
- Ocular artifacts
- Time constants
- Multi-channel recording
- Averaging
- Response identification
- Response components

**Psychological Aspects**
- Attention / Task relevance
- Probability / Expectancy
- Task difficulty
- Relation to reaction time

**Clinical Aspects**
- Clinical Applications
- Advantages / Limitations

**Physiological Aspects**
- Maturation / Development
- Sources / Generators
- Scalp Distribution
Running EEG/ERP studies

- Acquisition
  - Recording
  - Referencing
  - Amplification
- Statistical analysis
  - Averaging ERPs and difference waves
  - Site distribution
- Data interpretation
  - Source analysis
  - Identify cognitive correlates

Stimulation Technique

Simple Oddball Paradigm

- Stimuli differ on more than one dimension
- Multiple deviant stimuli
- Multiple target deviant stimuli

Complex Paradigms e.g.:
Stimulation Technique (Cont.)

Simple Paradigm

- Standards & deviants are stored / averaged in separate memories

Complex Paradigm

- Software should differentiate responses to standard or deviant(s)

Online Averaging

Offline Averaging

- Not available in most Current clinical Audiology equipment

Ocular Artifact Issues

- Electrical potentials generated by eye movements and blinks are a major problem when recording cortical potentials.

- EOG channel(s) is essential for dealing with this problem:
  - Reject from analysis any trials wherein eye movements occur, or
  - Subtract the ocular artifacts from the EEG
Multi-channel Recording

- Cortical potentials recording require the acquisition of multiple EOG/EEG channels:

- Waveform identification requires an indication of the general scalp distribution of the wave (minimum 4 appropriately placed channels 1EOG/3EEG)

- Investigating scalp topography of cortical responses require more channels (minimum 10 appropriately placed channels 1EOG/9EEG)
**Averaging**

- The more trials you average the more response amplitude you get, unless, the response is habituating

- 30-100 trials are enough for N2-P3

- 200 trials are minimum for MMN

**P3 Habituation**

![Graph showing brain responses to standard and deviant sounds with time (ms) and voltage (μV) axes.](image-url)
**Response Identification**

**N2-P3 Discriminative Cortical Potentials**

- Blue = 1000 Hz standard
- Red = 2000 Hz deviant

Pundy, Kelly & Davies (1995)

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**Response Identification**

**MMN**

Figure 1. The difference between ERPs to deviant and standard tone pips (averaged across 9 subjects) for the three electrode positions separately for the left (L) and right (R) ear when attended and when unattended. These difference curves were obtained by subtracting the corresponding time points of the ERP to standards from the ERP to deviants. I refers to Experiment 1 in which deviants were of higher frequency than standards, II to Experiment 2 where deviants were of higher intensity than standards. (From Näätänen et al., Acta Psychologica, 1978; reproduced with permission.)

Näätänen et al. 1978
Waveform Subtraction

Responses  Subtraction waves

Deviant – Standard

Fz  Lm

Brain’s response to the change in stimuli and/or task

Amplitude Measurement

- Peak-to-trough
- Relative to a pre-stimulus baseline (50-100 ms)
**Psychological Aspects**

**Relation to reaction time**

If one records RT simultaneously with auditory ERPs in simple oddball task, RT occurs 50 ms before P3 response.

**MMN Amplitude Variation**

**MMN as a Function of Frequency Change**

Sams et al. 1985
**Maturation / Development**

Microphone, speaker and video for communication with the patient

Mother positioned on the SARA system with the auditory stimulus delivery system attached.

**Maturational Effects - MMN**

- N=14 newborns
- Stimulus = /da/ versus /ta/

(Steinschneider et al, 1992)
**Maturational Effects — MMN**

Stimulus = 1000 vs 1200 Hz, 150 ms duration, ISI=750 ms

(Shafer et al 2000)

**Maturational Effects — N2-P3**

(Taylor 1988)
Generators

Cerebral Generators

- N1 (115 ms)
- MMN (185 ms)

Sources

- V
- 0.5, 0.2 μV
- CSD
- 0.25, 0.1 μV/cm²


Generators

Scalp potential distribution

EEG source current distribution

MEG source current distribution

160 ms
168 ms
176 ms
**P300 Protocol**

- **Stimulus**
  - tonebursts and/or speech phonemes
  - slow rate ≈ 1.1/s
  - duration 60-200 ms

- **Recording**
  - 0.1-30 Hz filter
  - F3, Fz, F4 positive electrodes for MMN
  - Cz, Fz positive electrodes for P3
  - earlobe or mastoid negative (reference) electrodes
  - 500-600 ms time window

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**MMN Recording**

- **Stimulus**
  - Tone bursts and/or speech phonemes
  - Slow rate ≈ 1.1/s
  - Rare < 20%
  - Duration 60-200 ms
  - SOA of 500 ms
  - Binaural presentation
  - Level of presentation of 70 dB nHL

- **Recording**
  - 0.1 - 30 Hz filter
  - F3, Fz, F4 positive electrodes are minimal for MMN recording
  - Earlobe or mastoid negative (reference) electrodes, Nose may be used.
  - 500 ms time window plus 100 ms pre-stimulus
Mismatch Negativity (MMN)

- MMN is a negative component of auditory ERPs evoked by a stimulus that differs (mismatch) from preceding stimuli.

- MMN is Change-detector response peaking at 100-200 ms from stimulus onset.

- This change may be in:
  - Single stimulus feature e.g. duration, intensity, frequency.
  - Spectrally complex stimuli e.g. phonemes.
  - Abstract changes in the relation between stimuli.

Mechanism of MMN
MMN Features

MMN has two distinctive features to make it a unique measure for evaluating the CANS:

- MMN has a definite relation to the auditory sensory memory.
- MMN is an automatic attention-independent response.

MMN and Sensory Memory

MMN provides evidence that stimulus features are separately analysed and stored in the vicinity of auditory cortex.

MMN provides a non-invasive, objective, task independently measurable physiologically correlate of stimulus-feature representations in auditory sensory memory.
MMN reflects automatic (pre-attentive) central auditory discrimination accuracy that correlates with perceptual accuracy.

MMN is also a likely component of the chain of brain events causing attention switches to changes in the environment.
Difficulties in recording

- The value of the signal is very small (3-5 uV) compared to the EEG.
- Individual recordings are not suitable for patients. Grand averaging is used.
- MMN occurs in the same latency range for other late AEPs, mainly N1-P2 complex.

Technical points in MMN recording

- **Calm EEG** is essential, so body or head movements should be totally avoided.
- **Subject’s attention** should be distracted by watching a silent movie or reading a book.
- **Number of rare stimuli** should not be less than 200. (with a 20% rare occurrence, this means 1000 total stimuli and minimal 1000 seconds)
- **Use a wide filter settings** (0.1 - 30 Hz) in recording, and tighten them in the peak identification process.
Clinical Applications of Discriminative Cortical Auditory Potentials

- Functional state of the cortex.
- Sensory and perceptual capabilities.
- Neural plasticity in the auditory system.
- Clinical audiological diagnosis.
1. Functional state of the cortex

Fischer, Morlet & Giard, Audiol Neurootol, 2000

Comatose patients

Normals
2. Sensory & Perceptual Abilities

Pekkonen, Audiol Neurootol, 2000
2. Sensory & Perceptual Abilities (Cont.)

Belal, Mourad, Sobhy, Aboras & Kozou, 2001

MMN in Aphasic patients

- Control subjects
- Aphasic patients

MMN in Aphasic patients

- Speech stimuli
- Non-speech stimuli
2. Sensory & Perceptual Abilities (cont.)

Grand-average MMNs

<table>
<thead>
<tr>
<th>Frequency change</th>
<th>Duration change</th>
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<tbody>
<tr>
<td>Right-ear stimuli</td>
<td></td>
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<tr>
<td>Patients</td>
<td></td>
</tr>
<tr>
<td>4 days</td>
<td>F3, F5</td>
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<tr>
<td>10 days</td>
<td>F3, F5</td>
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<tr>
<td>3 months</td>
<td>F3, F5</td>
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<tr>
<td>6 months</td>
<td>F3, F5</td>
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<td>Control subjects</td>
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<table>
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<th>Left-ear stimuli</th>
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<tr>
<td>Patients</td>
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<tr>
<td>4 days</td>
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<td>6 months</td>
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<td>Control subjects</td>
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Ilvonen, Kozou & Naatanen; 2003

3. Auditory Neuroplasticity

Discrimination Performance

Naatanen & Alho, Audiol Neurootol, 1997
4. MMN in Clinical Audiology

- Assessment of central auditory function
- Objective measure of auditory discrimination in infants and children
- Measuring residual speech discrimination in patients with auditory neuropathy
- May be predictive of cochlear implant (or hearing aid) performance
Grand average waveforms for small (20ms, red) and large (40ms, blue) gap deviants and standard stimulus (no gap, black) recorded at Fz. (Kelly et al., 2002)

Control group (n=10)  
APD group (n=8)

Grand average MMN for small (980 Hz, red) and large (1122 Hz, blue) frequency deviants compared to the standard (880 Hz, black) recorded at Fz. (Kelly et al., 2002)

Control group (n=10)  
APD group (n=8)
Effects of background noises on auditory processing

<table>
<thead>
<tr>
<th>Babble</th>
<th>Industrial</th>
<th>Traffic</th>
<th>Wide-band</th>
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**Speech stimuli**
- FZ

**Non-speech stimuli**
- FZ

Red: Noise
Green: Silent

Kazou, Shtyrov, Toppila, Alku, Kujala & Näätänen; 2003

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4. MMN in Clinical Audiology (con.)

**UNAIDED**

No MMN

**AIDED**

MMN

No Response

P1

Stapells, Oates & Kurtzberg, 2002
To conclude MMN...

- MMN reflects discrimination and memory in addition to sensation.
- MMN occurs automatically.
- MMN represents central auditory discrimination accuracy objectively.
- Clinically, it can be used in testing CAPD, sensory memory disorders, or general cognitive function in groups of patients.
- Improvements in the techniques and paradigms for eliciting MMN are needed before it can become clinically useful as an objective measurement of such disorders in individual patients.

P3 is an objective measure of CNS function

- Related to reaction time but occurs after physical response (ie, auditory processing continues)
- Substantial aging effects on P3 (latency ↑ by 1.5 msec per year)
- Abnormal in schizophrenia, Alzheimer's, alcoholism, learning disability associated with central auditory processing disorder, etc
P300 in neurological/psychiatric disease and aging

Polich et al., 2000

For example, "frequent" stimulus = 1000 Hz, and "rare" stimulus = 2000 Hz tone.
THANK YOU