

Discovering the relevant variables in a large
clinical database by back-fitting fixed effects in a
mixed linear model:
Study of a long-term electrophysiological survey
of cochlear implanted patients

Rafael Laboissière
Lyon Neuroscience Research Center, France

Rencontres R
Bordeaux
2012-07-03

(nominated for the Guinness book of records in the longest title category)

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- ▶ Eric Truy
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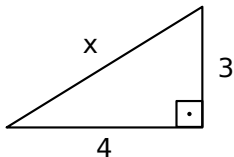
They are all physicians, I am the only “statistician.”

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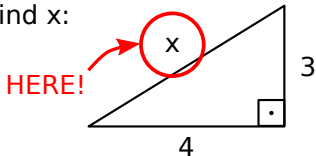


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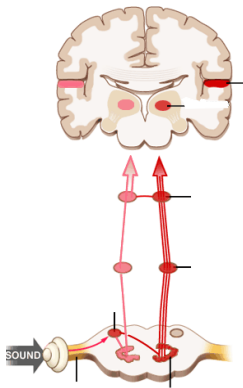
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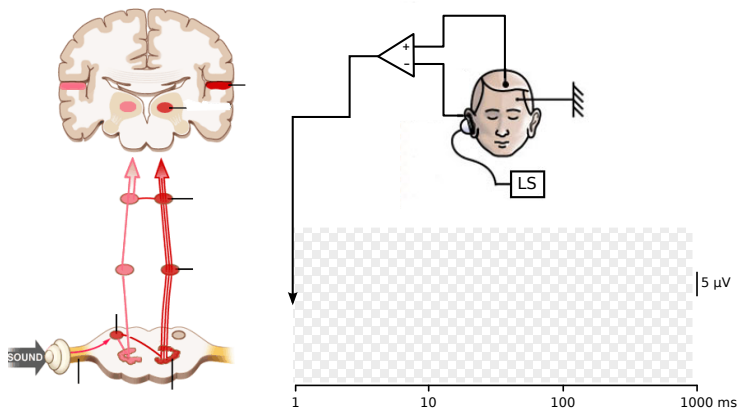


Auditory Evoked Potentials



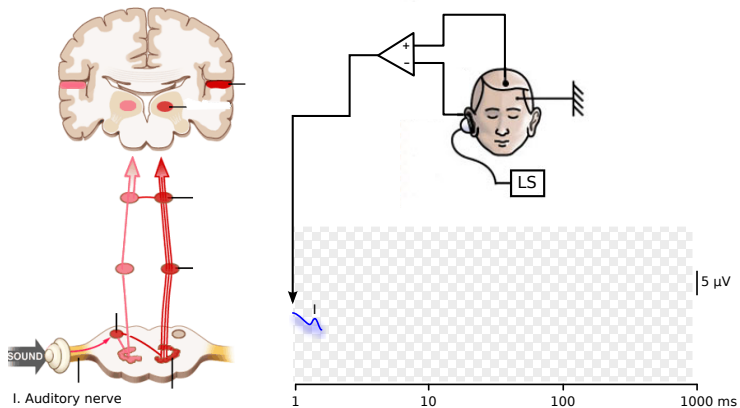
(drawing credits: <http://www.neuroreille.com>)

Auditory Evoked Potentials



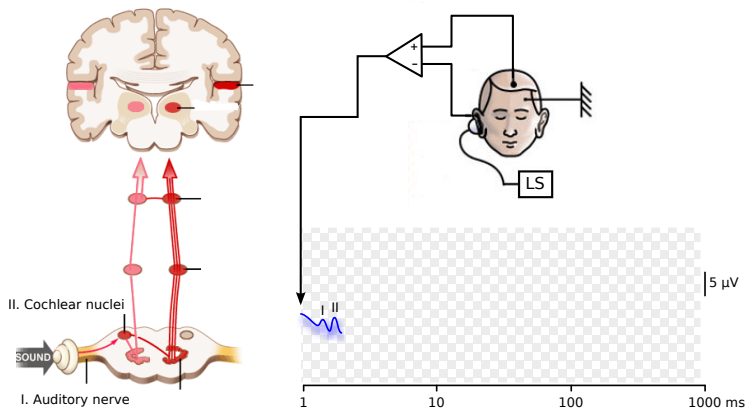
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Auditory Evoked Potentials



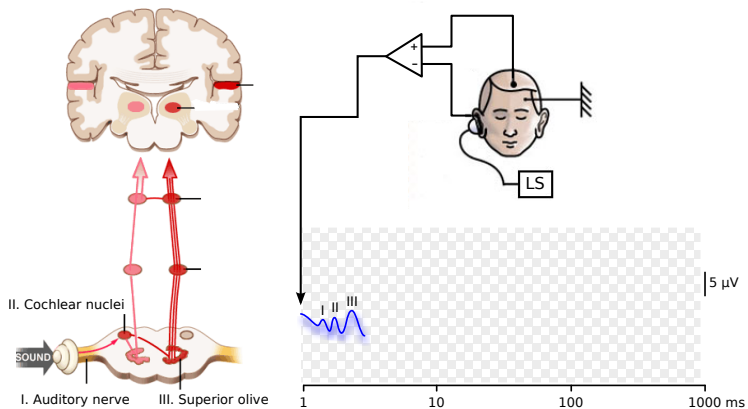
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Auditory Evoked Potentials



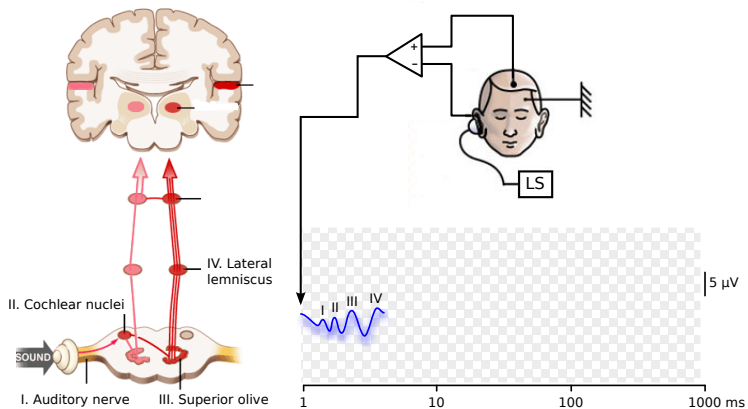
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Auditory Evoked Potentials



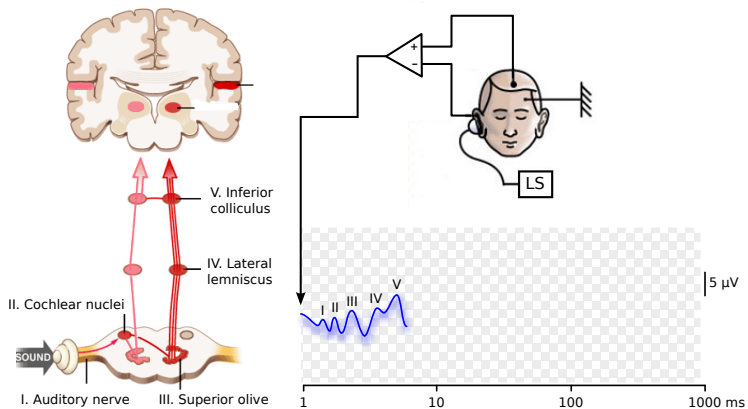
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Auditory Evoked Potentials



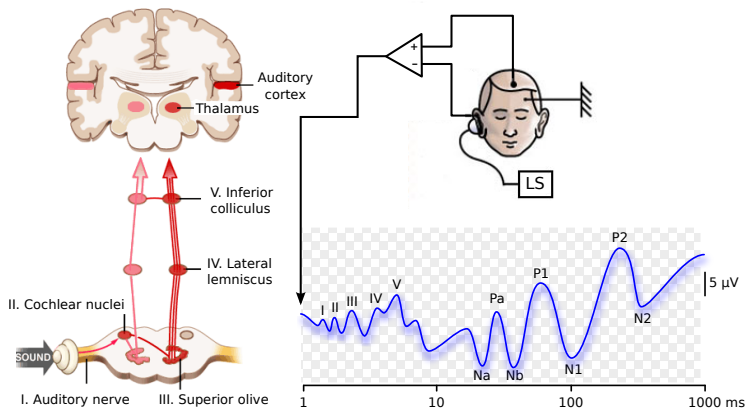
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Auditory Evoked Potentials



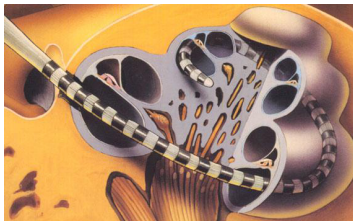
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Auditory Evoked Potentials



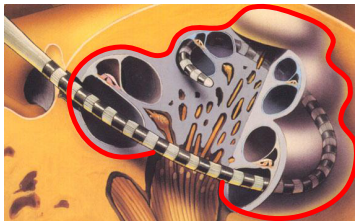
(drawing credits: <http://www.neuroreille.com>)

Cochlear Implant



(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

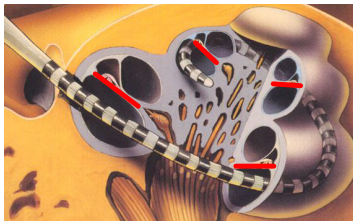
Cochlear Implant



cochlea

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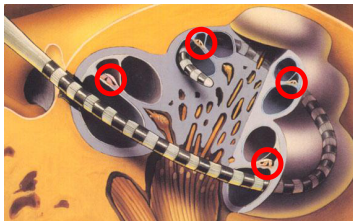
Cochlear Implant



basilar
membrane

(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

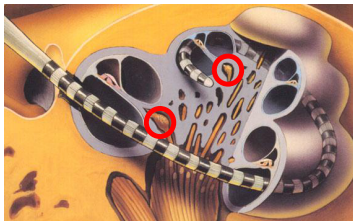
Cochlear Implant



organ
of Corti

(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

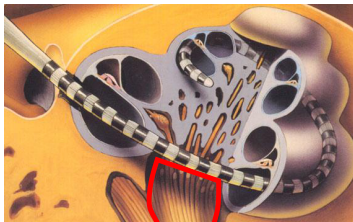
Cochlear Implant



spiral
ganglia

(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

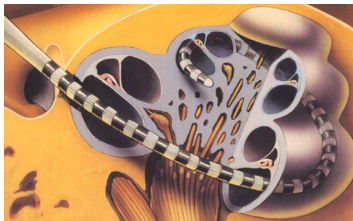
Cochlear Implant



auditory
nerve

(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

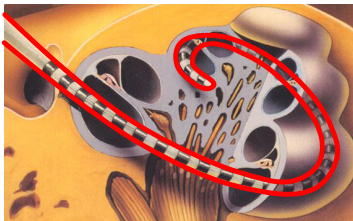
Cochlear Implant



profound deafness
=
death of the hairy cells

(pictures credits: <http://newspaper.li>, <http://www.cochlear.com>, and <http://entcentre.com>)

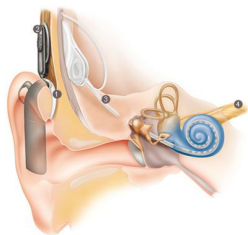
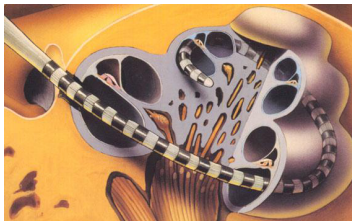
Cochlear Implant



electrode
array

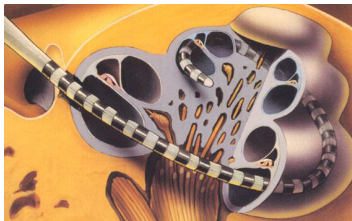
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Cochlear Implant

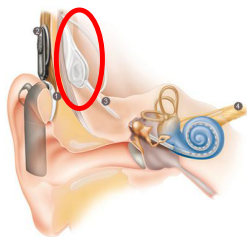


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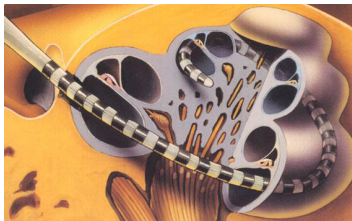


internal
antenna

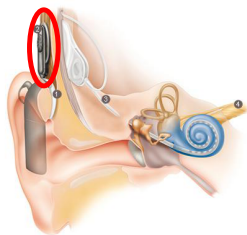


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Cochlear Implant

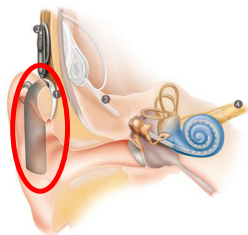
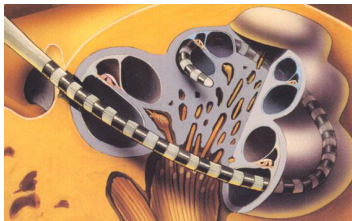


external
antenna



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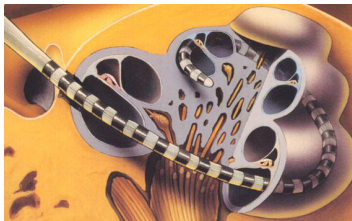
Cochlear Implant



microphone
& processor

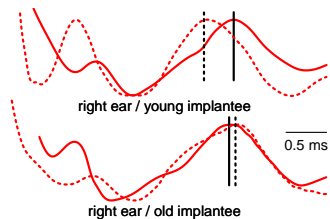
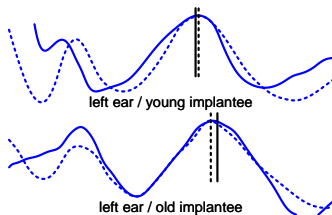
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Cochlear Implant



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Electrically Evoked Potentials



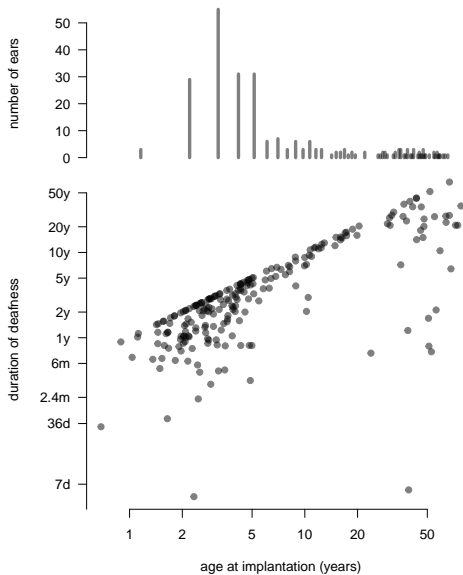
Variables and factors considered in this study

factor	variable	type	units
wave V latency	L_V	dependent variable	ms
wave III latency	L_{III}	dependent variable	ms
interval III–V	I_{III-V}	dependent variable	ms
duration of CI use	T	continuous factor	days
age at implantation	A	continuous factor	days
electrode	C	discrete factor	0: electrode 5 1: electrode 20
sex	S	discrete factor	0: female 1: male
ear side	E	discrete factor	0: right 1: left

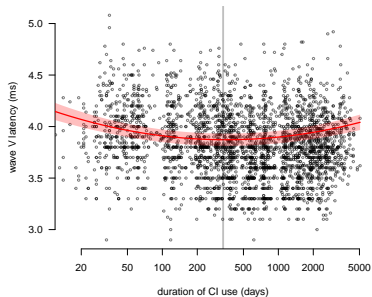
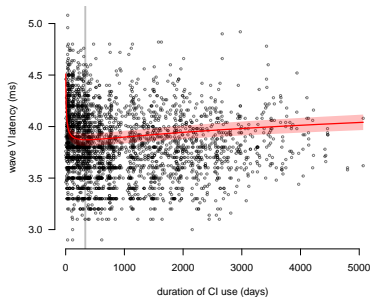
Side of implantation



Age at implantation and duration of deprivation



Raw data for wave V latency



Variables and factors considered in this study

factor	variable	type	units
wave V latency	L_V	dependent variable	ms
log duration of CI use	$\log(T)$	continuous fixed factor	$\log(\text{days})$
log duration of CI use sq.	$[\log(T)]^2$	continuous fixed factor	$\log(\text{days})^2$
age at implantation	A	continuous fixed factor	days
electrode	C	discrete fixed factor	0: electrode 5 1: electrode 20
sex	S	discrete fixed factor	0: female 1: male
ear side	E	discrete fixed factor	0: right 1: left
patient intercept		random factor	ms

LMERConvenienceFunctions package

Back-fitting of fixed effects (Newman et al., 2011; Tremblay and Tucker, 2011):

1. The F statistics of each factor for the fitted model is estimated.
2. Proceed from the highest-order interaction terms towards the individual factors.
3. The factor with the smallest value of F is considered for removal.
4. A statistical test is then made between the models with and without this factor by using the log-likelihood ratio test (LLRT).
5. If the resulting p -value is below a given threshold α , then the factor is kept, otherwise it is discarded.
6. Do it progressively until there are no factors left.

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LMERConvenienceFunctions package (cont.)

N.B.: If a factor is part of a higher-order interaction, it will be automatically included, regardless of the associated F value.

Finally, an ANOVA table of the reduced model is computed using conservative estimations of the degrees of freedom of the denominator.

LMERConvenienceFunctions package (cont.)

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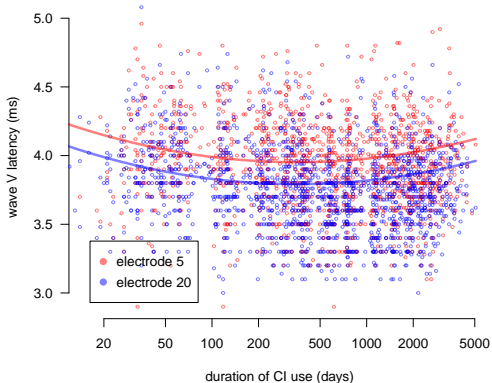
Finally, an ANOVA table of the reduced model is computed using conservative estimations of the degrees of freedom of the denominator.

Reduced model for wave V latency

$$\begin{aligned} L_V = & 5.4 - 0.157C + 0.11S - 1.8E + (-6 \times 10^{-2} + 0.16E) \log_2 A \\ & + [-0.32 + 0.27E + (10 \times 10^{-3} - 2.3 \times 10^{-2}E) \log_2 A] \log_2 T \\ & + 1.2 \times 10^{-2} (\log_2 T)^2 \end{aligned}$$

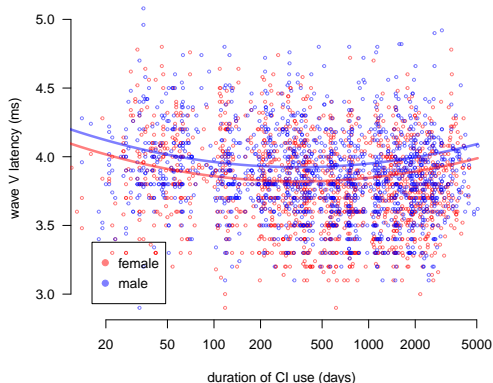
Electrode effect

$$L_V = 5.4 - 0.157 C + 0.11S - 1.8E + (-6 \times 10^{-2} + 0.16E) \log_2 A \\ + [-0.32 + 0.27E + (10 \times 10^{-3} - 2.3 \times 10^{-2} E) \log_2 A] \log_2 T \\ + 1.2 \times 10^{-2} (\log_2 T)^2$$



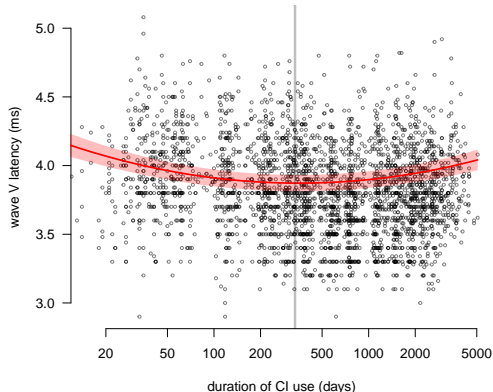
Sex effect

$$L_V = 5.4 - 0.157C + 0.11S - 1.8E + (-6 \times 10^{-2} + 0.16E) \log_2 A \\ + [-0.32 + 0.27E + (10 \times 10^{-3} - 2.3 \times 10^{-2}E) \log_2 A] \log_2 T \\ + 1.2 \times 10^{-2}(\log_2 T)^2$$



Quadratic dependency on the duration of CI use

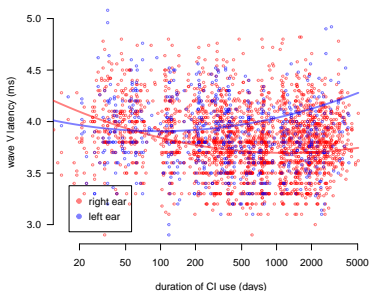
$$L_V = 5.4 - 0.157C + 0.11S - 1.8E + (-6 \times 10^{-2} + 0.16E) \log_2 A \\ + [-0.32 + 0.27E + (10 \times 10^{-3} - 2.3 \times 10^{-2}E) \log_2 T] \log_2 T \\ + 1.2 \times 10^{-2} (\log_2 T)^2$$



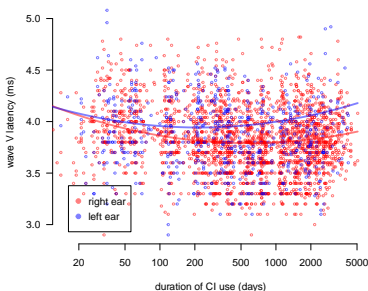
Ear \times age at implantation \times duration of CI use

$$L_V = 5.4 - 0.157C + 0.11S - 1.8E + (-6 \times 10^{-2} + 0.16E) \log_2 A \\ + \left[-0.32 + 0.27E + (10 \times 10^{-3} - 2.3 \times 10^{-2} E) \log_2 A \right] \log_2 T \\ + 1.2 \times 10^{-2} (\log_2 T)^2$$

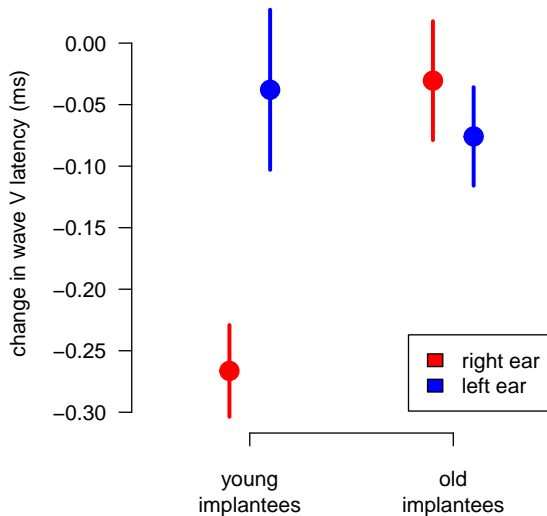
young implantee (251 days)



old implantee (3.9 years)



Age-matched cohort, partitioned groups



Thank you for your attention.