Auditory Verbal Hallucinations

Hallucination Consortium 2014
Trondheim
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What are auditory verbal hallucinations (AVH)?

- Hearing speech, while there is no source for it.
- The speech is not recognized as self derived.
- This is a perceptual phenomenon, not just thoughts or ideas.
- Voices can be heard inside or outside the head.

Sommer et al. Psychopathology 2010
Who experience AVH?

- Most characteristic for psychosis
- In other psychiatric conditions (affective disorders, personality disorders, PTSD, dissociation, autism etc)
- In temporal lobe epilepsy
- In hearing loss (auditory variant of Charles Bonnet syndrome)
- In some 4-30% of healthy individuals

Sommer et al. Neuropsychiatry 2012
The voices tell me to commit suicide.
Frequent AVH in a healthy person
Negative content specific for AVH in psychosis

- when >50% of voices have negative emotional content: >82% chance for psychotic disorder
- when all voices have negative content: >90% chance for psychotic disorder
- Content of voices should be asked in all diagnostic interviews!!

Brain equivalents of AVH

Measuring brain activation during voices

3T MRI scanner

Patient indicates voices

Scan sequence:
3D-PRESTO pulse sequence
with parallel imaging (SENSE) in 2 directions

Neggers et al. NMR Biomed 2008
Brain activation during AVH

Single subject
Groupwise analysis, n=24
activation during AVH

bilateral insula, right homologue of Broca’s area

Right supramarginal gyrus

right superior temporal gyrus and Broca’s homologue

Sommer et al. Brain 2008
Normal language production
same 24 patients

Broca and bilateral insula
Wernicke left > right
Anteriore cingulate gyrus
Activation during AVH in patients with psychosis and healthy subjects

psychotic patients, n=21

non-psychotic individuals, n=21

Diederen et al. Schizophrenia Bulletin 2011
Results conjunction analysis

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Regions</th>
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<tbody>
<tr>
<td>152</td>
<td>L postcentral gyrus/ supramarginal gyrus</td>
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<tr>
<td></td>
<td>L precentral gyrus/ superior temporal gyrus</td>
</tr>
<tr>
<td></td>
<td>L inferior parietal lobule</td>
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<tr>
<td>13</td>
<td>R superior temporal/ inferior frontal/ insula</td>
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<tr>
<td>20</td>
<td>Left Inferior Frontal/ Insula/ Superior Temporal</td>
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<tr>
<td>7</td>
<td>R Postcentral/ Supramarginal</td>
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<td>5</td>
<td>R Cerebellum</td>
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</tbody>
</table>
Results two samples t-test

Non-psychotic vs psychotic

→ No significant differences

Diederen et al. Schiz Bull 2011
Fasciculus arcuatus

Important connection between frontal and temporo-parietal areas
Provides very fast communication between language areas
Magnetic Transfer Ratio
Measures disturbances in proton magnetic resonance caused by macromolecules (myeline among others) but also sensitive to free water because of long T1 time.
Quality of the arcuate fasciculus

Both psychotic patients and healthy subjects with AVH have higher MTR values, which suggests increased free water. This may indicate a lower quality and slower communication between language areas.

De Weijer et al. Human Brain Mapping 2011
What triggers AVH?

- Patient experiences voices
- 6-0 seconds before the voices

Statistics:
Finite Impulse Response functions (FIR)
10 FIR timebins of 0.609s = interscan interval tailored 'selective averaging'
Largest signal changes preceding AVH

(para) hippocampus

p<0.05 whole-brain corrected by the false discovery rate (FDR)

Diederen et al. Am J Psychiatry 2010
Conclusions from MRI studies

- During hallucinations activation in language perception and production areas
- Activation lateralized to the right hemisphere
- Slightly lower quality of arcuate fasciculus
- Preceded by signal change in (para) hippocampus; may be triggered from memory
Treatment for voices

- fMRI scans used for psycho-education
- Improve coping
- Individual psychotherapy
- Optimise medication
- Group therapy
- Experimental treatment
Copings strategies:

Top 10 Voices Clinic UMCU

1. Having a conversation 73%
2. Singing/ Humming 70%
3. Whisteling 60%
4. Reading aloud 50%
5. Sleeping 43%
6. Listening to the radio 30%
7. Shouting 28%
8. Reading 30%
9. Chewing gum 25%
10. Hobby's: internet, sports etc 16%
Effects of anti-psychotic medication on voice hearing

Eufest sample, n=362
Psychotherapy for voice hearing

- Prevent that patients carry out dangerous assignments from the voices (mainly with behavioral therapy)
- Lower delusional beliefs regarding source and power of the voices (CBT)
- Lower the emotional impact of the voices (COMET)
- Improve self-confidence (COMPASSION training)
Treatment for voices

- fMRI scans used for psycho-education
- Improve coping
- Individual psychotherapy
- Optimise medication
- Group therapy
- Experimental treatment
Possibilities of TMS

- Can influence focal brain activity
- Few side effects
- Safe

Impossibilities of TMS

- Cannot reach deep areas
- Effects short lasting
- Not very precise
TMS can alleviate medication-resistant AVH


Temporalparietal transcranial magnetic stimulation for auditory hallucinations: safety, efficacy and moderators in a fifty patient sample.

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Abstract

BACKGROUND: Auditory hallucinations are often resistant to treatment and can produce significant distress and behavioral difficulties. A preliminary report based on 24 patients with schizophrenia or schizoaffective disorder indicated greater improvement in auditory hallucinations following 1-hertz left temporoparietal repetitive transcranial magnetic stimulation (rTMS) compared to sham stimulation. Data from the full 50-subject sample incorporating 28 new patients are now presented to more comprehensively assess safety/tolerability, efficacy and moderators of this intervention.

METHODS: Right-handed patients experiencing auditory hallucinations at least 5 times per day were randomly allocated to receive either rTMS or sham stimulation. A total of 132 minutes of rTMS was administered over 9 days at 90% motor threshold using a double-masked, sham-controlled, parallel design.

RESULTS: Hallucination Change Score was more improved for rTMS relative to sham stimulation ($p = .008$) as was the Clinical Global Impressions Scale ($p = .0004$). Hallucination frequency was significantly decreased during rTMS relative to sham stimulation ($p = .0014$) and was a moderator of rTMS effects ($p = .008$). There was no evidence of neurocognitive impairment associated with rTMS.

CONCLUSIONS: Left temporoparietal 1-hertz rTMS warrants further study as an intervention for auditory hallucinations. Data suggest that this intervention selectively alters neurobiological factors determining frequency of these hallucinations.
Activation during AVH

- Varies highly between patients
- Wernicke’s area is not always involved
- Half the patients activate predominantly the right hemisphere during AVH
fMRI-guided TMS

1. fMRI: localise brain activity during hallucinations

2. Neuro Navigator: find exact spot overlying fMRI hotspot

3. TMS: decrease focal brain activity
   1Hz, 20 minutes, 15 days
Brain activity during AVH

Hallucination “hotspot”: activation map divided in separate clusters of voxels. Average beta value from each cluster multiplied by the #voxels of that cluster. In cluster with highest multiplication value, voxel with highest T value assigned as target coordinate.
How reliable is fMRI to detect hallucination hotspots?

- Test-retest scans during hallucinations of 33 patients
- Measure activation pattern and calculate hallucination hotspot twice
- Calculate mean distance between hallucination hotspot scan 1 and scan 2
Test-retest results

Mean distance between hotspot 1 and 2: < 2cm for all brain regions

Abbreviations: ITP, left temporoparietal area; lMT, left motor area; rIF, right inferior frontal area; mSF, middle superior frontal area; rCB right cerebellum
Design RCT

117 pt with intractable AVH all had fMRI scans
62 valid activation patterns
Randomisation

- 20 fMRI-guided TMS
- 22 non-guided TMS
- 20 sham treatment

All groups: 1Hz, 90%MT, 20 minutes 15 sessions

fMRI-guided TMS: at hallucination hotspot
Non-guided TMS: at left temporo-parietal cortex
Sham TMS: at fMRI hotspot TMS coil tilted 90°
fTMS treatment for AVH

n=62

Dr. Karin Slotema

Severity of hallucinations

AHRS

Week 1
Week 2
Week 3
FU 1 month
FU 2 months
FU 3 months

fMRI
non-guided
sham

Slotema et al. Biological Psychiatry 2011
Results fMRI guided TMS

- All three groups improved significantly
- No significant differences in efficacy between the three groups
- When fMRI-guided group and non-guided TMS group are pooled they are still not significantly better than sham

Conclusion: 1Hz TMS stimulation protocol not effective in this study!
### Meta-analysis of 17 1Hz TMS studies for AVH

<table>
<thead>
<tr>
<th>Study name</th>
<th>Subgroup within study</th>
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<th>p-Value</th>
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**Meta Analysis**

Slotema et al. Schizophrenia research 2012
Effect sizes versus year of publication

![Graph showing the relationship between effect size and study year. The R² Linear value is 0.318.](image-url)
Priming TMS n=23
(first 5 minutes at 6Hz)

Slotema et al. Brain Stimulation 2012
Other strategies for focal stimulation

- More effective TMS stimulation paradigms: for example burst frequencies
- More effective TMS coils, such as H-coil
- Direct current stimulation
To be continued…

Thank you for your attention!

UMC Utrecht, Neuroscience Division
Iris Sommer
Kelly Diederen
Antoin de Weijer
Kirstin Daalman
Bas Neggers

Parnassia-Bavo Group
Jan Dirk Blom
Karin Slotema
Rutger Goekoop
Wijbrand Hoek