Mapping language in the human brain: Evidence from aphasia.

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Functional Neuroimaging studies:
- identify brain structures underlying language tasks / functions
- Correlations between neural systems and intact language performance

Ideally, conclusions should converge

Neuropsychological studies of brain and language:
Clinical syndromes (behaviour)
Topography of brain damage (structure)
Identify brain areas necessary for language

Neuropsychologists approach to brain and language
1. Explain the patterns of impaired and intact language performance seen in brain injured patients in terms of damage to one or more components of a theory of normal cognitive functioning
2. Draw conclusions about normal, intact language processes from the patterns of impaired and intact capabilities seen in brain injured patients
(adapted from Ellis and Young, 1988)

Historical and classical aphasias:
Clinical syndromes (behaviour)
Topography of brain damage (structure)

Left-brain, Right-brain
- Language damage far more likely following left-hemisphere damage
- Left-hemisphere dominance for language if right handed
- Not so true in left-handers (around 30% show switched dominance)
Broca's Aphasia
(non fluent aphasia)

- Identified 1861 by Paul Broca, a Parisian neurologist
- Patient "Tan":
  1. intelligent,
  2. good language comprehension,
  3. severe deficit in speech production
- Died soon afterwards: brain showed selective damage at frontal lobe, left hemisphere

Cerebral anatomy

Wernicke's Aphasia
(Fluent Aphasia)

- Identified 1873 by Carl Wernicke, German neurologist
- Patient with
  1. reasonably good speech,
  2. very poor language comprehension
- Died soon afterwards: brain showed selective damage in rear parietal/temporal region, left hemisphere

Cerebral anatomy
Case 2: SH

QuickTime™ and a YUV420 codec decompressor are needed to see this picture.

In the dominant hemisphere

- **Broca’s Area**: responsible for speech production (close to motor areas)
- **Wernicke’s Area**: responsible for speech comprehension (close to auditory areas)

Wernicke /Litcheim Model

<table>
<thead>
<tr>
<th>Speech input</th>
<th>Wernicke’s area (word sound centre)</th>
<th>Broca’s area (speech output centre)</th>
<th>Speech output</th>
</tr>
</thead>
</table>

Arrows indicate tracts joining language centres

Cerebral anatomy

- **arcuate fasciculus**
- **Broca’s Area**
- **Broca’s Aphasia**
- **Wernicke’s Area**
- **Wernicke’s Aphasia**
Striking confirmation: Conduction Aphasia

- Damage to Arcuate Fasciculus -- a tract of fibers connecting BA and WA
- Patients show:
  1. good comprehension,
  2. good production,
  3. poor repetition.

In Broca’s and Wernicke’s day: Definitive Diagnosis...

Current position

- Aphasia is not just a question of fluent/ non-fluent speech
- Very rare to get patients with isolated speech production or comprehension deficits (relative damage)
- Multiple interconnected cognitive levels of language processing
- Detailed cognitive assessment of the patient can give valuable insights into the nature of the underlying linguistic damage.

A current model of language processing

Neuropsychological studies:

- If a lesion causes a specific language deficit according to model, then the lesioned area must be necessary for that language function
- Behavioral impairment provides critical information about the nature of the cognitive deficit

- Limitations,
  Neuropsychological profiles tend to be complicated, with patients having more than one cognitive deficit not always clear dissociations of functioning
  - Some brain regions are immune from ischemic damage (thus can’t be investigated)

Neuroimaging studies of brain and language:

Language performance on specific cognitive task

Neural correlates of performance
  (i.e. Brain areas activated by/correlated with specific task)
Imaging in aphasia

Structural
  CT
  MRI
  TI, T2, FLAIR

Functional (Research)
  SPECT
  PET
  fMRI
  Volumetric

Functional Imaging studies:
- Used mostly in normal subjects to investigate the principal of functional segregation (i.e., different brain regions serve different functions)
- A hierarchy of tasks can be used to isolate specific cognitive functions (e.g., investigate the neural correlates of written word processing by assuming that reading goes through a single series of discrete and independent stages. By comparing responses to a hierarchy of stimuli (e.g., false fonts vs. letters; letter strings vs. words, etc.), each stage is associated with a different brain region.)
- A variety of tasks can be used to activate each brain region (even those that are immune from ischemic damage)

Inferences:
If a set of regions activate during a cognitive task, then these brain regions must be sufficient for that task performance.

Interpreting Activations in Normals

<table>
<thead>
<tr>
<th>Unsuccessful Task Performance</th>
<th>Successful Task Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No activity</td>
<td>The region is not necessary for task performance</td>
</tr>
<tr>
<td>Activity</td>
<td>The region is sufficient for task performance</td>
</tr>
</tbody>
</table>

Interpreting Activations in Patients, compared with control group (Normals)

<table>
<thead>
<tr>
<th>Impaired Task Performance</th>
<th>Preserved Task Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underactivity</td>
<td>The region is not necessary for task performance</td>
</tr>
<tr>
<td>Overactivity</td>
<td>Cognitive or neuronal reorganization</td>
</tr>
</tbody>
</table>

The 2 different approaches: applied to aphasia

1) While neuropsychological studies identify the regions that are necessary for the lost language function, PET and fMRI studies can identify complete set of regions sufficient for one language task relative to another

2) While neuropsychological studies can be used to investigate aphasic patients, impaired language function) PET and fMRI studies can only be used with normals or patients that can perform the task to some extent.

Thus, behavioral impairment on a task precludes the investigation of neuronal responses for that task.

Ideally, conclusions about brain and language should converge

Lesion Studies Inferences:
If damage to area 1 impairs function A, area 1 is involved in A

Example 1:
If damage to Wernicke’s area impairs function speech comprehension, Wernicke’s area is involved in speech comprehension.
Studied 24 aphasics following left hemisphere stroke

- **T-group**
  - \( n = 6 \)
- **T+ group**
  - \( n = 18 \)
- **Wernicke’s group**
  - \( n = 9 \)

- No difference: Age (T- = 60; T+ = 65; \( p = 0.4 \))
- Time of study after infarct (T- = 58; T+ = 24 months; \( p = 0.1 \))
- Studies performed at 3-120 months post stroke

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### Behavioural Data

<table>
<thead>
<tr>
<th>Aphasia Group</th>
<th>Auditory Word comprehension Mean</th>
<th>S.E.</th>
<th>Auditory Sentence comprehension Mean</th>
<th>S.E.</th>
<th>Written Word comprehension Mean</th>
<th>S.E.</th>
<th>Written Sentence comprehension Mean</th>
<th>S.E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temp-</td>
<td>27.6</td>
<td>.97</td>
<td>26.4</td>
<td>1.93</td>
<td>28.4</td>
<td>.81</td>
<td>27.1</td>
<td>1.41</td>
</tr>
<tr>
<td>Temp+</td>
<td>23.7</td>
<td>.99</td>
<td>15.7</td>
<td>1.67</td>
<td>26.1</td>
<td>.94</td>
<td>16.1</td>
<td>3.11</td>
</tr>
<tr>
<td>Wernicke’s</td>
<td>24.5</td>
<td>1.41</td>
<td>14.9</td>
<td>1.76</td>
<td>26.9</td>
<td>.96</td>
<td>19.7</td>
<td>2.70</td>
</tr>
<tr>
<td>Max.</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

*At a group level impaired speech comprehension was predicted by whether pts had a left temporal lobe lesion or not. Size of the lesion didn’t predict speech comprehension deficits, i.e. There was no significant difference between those patients who had isolated Wernicke’s lesions or more extensive Temp + lesions on tests of speech comprehension.*

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**Aphasia post stroke:**

**Lesion overlap from CT scans**

- Diagram of four ischemic lesions in the lower division of the left middle cerebral artery territory, illustrating typical patterns of lesion overlap (dark shading).
- Lesion did not predict language performance nor vice versa.

Despite common area of cortical damage individual patients had recovered speech comprehension to varying degrees.

*Need functional imaging of patients*

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**Functional imaging of neurologically normal subjects**

- **Listening to Stories (St) > Reversed Stories (RSi)**

(\( Z \)-score >4.8, \( P < 0.05 \) corrected)

\( n = 11, \text{ age: 37-76 yrs} \)
Hypotheses

- Increasing evidence in monkeys and man that speech comprehension may be a function of anterior projections:
  - Auditory information projects from Auditory Cortices (Wernicke’s area) along the length of the STG and dorsal bank of the STS.
- Patients with posterior lesions involving left Wernicke’s area can have speech comprehension deficits:
  - Not only due to the cortical damage itself
  - But also at least in part, attributable to reduced function in the ipsilateral anterolateral temporal cortex, due to the impaired input from Wernicke’s area.
- This anterior superior temporal region and its function may have been missed from classical lesion studies as selective damage here following aphasic stroke is rare.

Vascular lesions

- Respect vascular boundaries not functional ones and are a combination of gray and white matter damage in the network.

Need functional imaging of patients

Summary Example 1:

- Vascular lesions involve both cortical gray and white matter damage and result in disconnection (anatomical and functional) so they preclude a simple one to one mapping of structure and function.
- Common deficits in a group of aphasic stroke patients that are “task-specific” (sentence speech comprehension) do not necessarily imply a unique common task-specific brain region.
- Task-specific deficits can arise from differences in the interactions among a common network of brain regions.

- Thus we may characterize speech comprehension deficits:
  - Not as resulting from a lesion in a single Wernicke’s area,
  - But rather as result of a lesion affecting a functional network involving left anterior and posterior superior temporal areas,
  - With each left superior temporal region contributing to speech comprehension processing.

- Inferences from lesion studies (using aphasic stroke patients) need to be constrained by Functional Imaging Data.
**Functional imaging Inferences:**

If area 1 is activated by a task then it is involved in that task.

If a patient has a lesion to 1 but can still do the task that area is not necessary. i.e., the residual areas within the neural system can be sufficient.

**Example 2:**
The left temporal lobe is activated by speech comprehension tasks and is involved in that task (Example 1).

If a patient has a lesion to the left temporal lobe but still has good speech comprehension, the left temporal lobe is not necessary. i.e., the residual areas within the neural system (i.e., right anterior temporal lobe) can be sufficient.

As seen in Example 1, lesion studies can be consistent.

**Functional imaging**

Speech comprehension

**Lesion (VBM)**

Impaired comprehension

Other lesions to this system do not impair sentence comprehension.

**Functional imaging**

Speech comprehension

**VBM**

All left superior temporal cortex can be destroyed without disrupting sentence comprehension.

To explain why speech comprehension is intact, we need functional imaging of the patient...
**Functional imaging: Patient Variability**

Norm group (18 subjects)

Looks abnormal

But...

Patient responses are all within normal range

**Functional imaging: Normal variability**

Norm group (18 subjects)

Looks abnormal

But...

Patient responses are all within normal range

**Activation increases with auditory sentence comprehension score**

Comprehension score vs. Comprehension score

**Summary Example 2:**

- Damage to the normal neural system & good performance indicates alternative processing strategies for the same task
- Alternative processing strategies for the same task precludes a one to one mapping of structure and function
- Speech comprehension relies on a distributed system across both the left and the right temporal lobes
- Individual variability within the normal population may determine whether and how a patient recovers from cortical damage
- Inferences from Functional Imaging studies (using normal subjects) need to be constrained by Lesion data

**Do conclusions converge?**

- Example 1 showed impaired speech comprehension is predicted by side of the effect (St>RSt) in left anterior STS following Wernicke’s area infarction
- Example 2 showed good speech comprehension is predicted by correlation between speech comprehension and right anterior STS activity following left temporal lobe infarction

However, characterising brain activity in terms of functional segregation i.e. where in the brain different cortical regions serve different functions does not reveal anything about how different brain regions communicate with each other.

Critically, both studies rely on the assumption that different brain areas communicate with each other i.e. the neural correlates of semantic processing during speech can be identified using spoken narratives by virtue of the assumption that auditory regions interact with semantic regions.

**Functional Connectivity Study: Example 3**

In common to both examples 1 and 2 was

- activation in right anterior STS for the contrast St>RSt

**Hypothesis:**

- It is a change in coupling (connectivity) between right and left anterior STS that explains the behavioural difference between patients with good speech comprehension and those with impaired function
Connectivity and behaviour
Significant correlation between LaSTS-RaSTS correlation strength and auditory single word comprehension scores

$p < 0.05$

Connectivity and behaviour
Significant correlation between LaSTS-RaSTS correlation strength and auditory sentence comprehension scores

$p < 0.05$

Summary Example 3:
In a group of aphasic stroke patients with intact left and right anterior superior temporal cortex

- The strength of LaSTS – RaSTS connectivity predicted performance on tests of auditory single word and sentence comprehension
- No significant relationship between correlation strength and performance for tests of written comprehension – effect restricted to auditory comprehension
- Both left and right anterior superior temporal cortices are important for speech comprehension
- Variability in the strength of bilateral anterior connections (structurally intact regions) must be dependent on ‘noise’ of input from posterior regions (Wernicke’s area)

Conclusions from examples 1 and 2 do converge

Overall Summary:
- Positive and negative predictors for language impairments are not just about the lesion location
  
  Example 1
- Different normal language functions involve different neural networks and may have different capacities for recovery
  (? Related to Normal variability in the neural systems involved in any 1 function)  
  Example 2
- In pt studies we need to consider how a lesion impacts on neural networks ipsilateral and contralateral to the lesion (anatomical and functional connections)  
  Examples 1 and 3 need to combine Neuropsychological and Functional imaging data

Relationship between clinical symptom, location of pathology and neural correlates of language is not a simple one

Clinical symptoms (language behaviour)  

Topography of brain damage (structure)  

Neural correlates (function)

And what about reorganisation??.....

Examples 3 & 4:
Recovered patients with a Wernicke’s area stroke (left posterior Superior Temporal Sulcus) demonstrated an increase in response in their right pSTS.

Example 3

- Patients with damage to left hemisphere regions had increased activation in the right hemisphere homologues when compared to normal subjects and patients whose lesions spared that network.
- As a group activation in the right hemisphere region contralateral to the lesion did not predict the patient's performance on language tests.

Conclusions:
- A left hemisphere stroke does not mean general reorganisation of all language networks.
- While the left hemisphere may be dominant for language the right hemisphere may also play a role.

Example 4: Speech production

Patients with damage to left Broca’s area had increased activation in the right hemisphere homologues when compared to normal subjects and patients whose lesions spared that network.

As a group activation in the right hemisphere region contralateral to the lesion did not predict the patients’ performance on speech production tests.

Conclusions: Examples 3 & 4

- Following damage to the certain speech systems patients do appear to have increased signal in the right hemisphere homologues - evidence for functional plasticity.
- What these differences in right hemisphere activations mean remain to be answered - as there were no behavioural correlations between the abnormal signal and language skills.
  (It could be facilitatory or inhibitory to language recovery.)
Overall Summary:
- Positive and negative predictors for language impairments are not just about the lesion location. Example 1.
- Different normal language functions involve different neural networks and may have different capacities for recovery. (Related to Normal variability in the neural systems involved in any function) Example 2.
- Consider impact of lesion on neural networks ipsilateral and contralateral to the lesion (anatomical and functional connections), and change longitudinally over time (plasticity) Examples 3 & 4.

Mapping language in the human brain:
- There is a strong correlation between brain structure and language performance but the relationship is not a simple one.
- Neuropsychological data and Functional imaging data need to be combined.

References:

Next step: Combining neuropsychology and neuroimaging to inform treatment?
- Following aphasic stroke cortical areas that display abnormal function may be a target for intervention.
- Targeted behavioural /pharmacological treatments need to be developed and evaluated.
- Potentially maximum outcomes for language recovery after stroke will be different treatment approaches for different aphasic symptoms.

More about the aphasia research?
- Cross sectional studies of monolingual and bilingual aphasics:
  - Speech comprehension
  - Speech production
  - Reading
- Longitudinal studies of aphasia recovery

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