Learning from rarities/oddities in nature

Main Points
1. Even injury is dynamic process
2. Intervention possible at many levels
3. Balance between specialization/differentiation and plasticity

Study questions
1. What factors influence the behavioral/cognitive outcome of a neurological injury? Give as many different kinds of answers as possible.
Why might studying arctic ground squirrels help treatment of brain trauma?
Your friend in his 20’s is at a party and is having trouble getting words out and the right side of his body is numb and weak. What should you do?
A. Ask if he wants help and do what he wants
B. Take away his keys and put him to bed
C. Post embarrassing videos of him on facebook
D. Wait a few hours and if symptoms persist, take him to the doctor
E. Get to the emergency room immediately
The person described in the last question has very likely suffered from

A. Stroke
B. Epilepsy
C. Drunkenness
D. Heart attack
E. Narcolepsy
Kinds of brain injury in adulthood

Stroke -- loss of blood supply

2nd leading cause of death

Leading cause of adult disability

½ of survivors dependent on others for daily living
Ischemic - clots
Hemorrhagic – bleeding
MRI of a patient who has had a stroke of the left hemisphere of the brain. The arrow indicates the area that was affected.

CT scan of a patient who has had a left middle cerebral artery stroke. The arrow indicates the location of the stroke.
NIHSS Results

1a - Level of Consciousness
1b - LOC Questions
1c - LOC Commands
2 - Best Gaze
3 - Visual Fields
4 - Facial Palsy
5a - Left arm
5b - Right arm
6a - Left leg
6b - Right leg
7 - Limb ataxia
8 - Sensory
9 - Best Language
10 - Dysarthria
11 - Extinction

NIHSS Score: 7
Association of laterality and size of perfusion lesions on neurological deficit in acute supratentorial stroke

Meng Lee, Jeffrey L. Saver, Jeffry R. Alger, Qing Hao, Noriko Salamon, Sidney Starkman, Latisha K. Ali, Bruce Ovbiagele, Dojin Kim, J Pablo Villablanca, Michael T. Froehler, Matthew S. Tenser, David S. Liebeskind

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Table 1. Characteristics of first-ever right-handed left and right-hemisphere stroke patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Left-hemisphere stroke, n = 58</th>
<th>Right-hemisphere stroke, n = 53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>64.5 (interquartile range 50–79)</td>
<td>65 (interquartile range 59–78)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>30 (52%)</td>
<td>19 (36%)</td>
</tr>
<tr>
<td>NIHSS score</td>
<td>10 (interquartile range 4–19)</td>
<td>8 (interquartile range 3–14)</td>
</tr>
<tr>
<td>Ischaemic volume (ml)</td>
<td>53 (interquartile range 26–92)</td>
<td>65 (interquartile range 32–120)</td>
</tr>
<tr>
<td>Time interval between LNW to PWI (minutes)</td>
<td>350 (interquartile range 250–520)</td>
<td>390 (interquartile range 260–540)</td>
</tr>
<tr>
<td>Category</td>
<td>Score/Description</td>
<td>Date/Time Initials</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>1a. Level of Consciousness</td>
<td>0 = Alert</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = Drowsy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Stuporous</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = Coma</td>
<td></td>
</tr>
<tr>
<td>1b. LOC Questions</td>
<td>0 = Answers both correctly</td>
<td></td>
</tr>
<tr>
<td>(Month, age)</td>
<td>1 = Answers one correctly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Incorrect</td>
<td></td>
</tr>
<tr>
<td>1c. LOC Commands</td>
<td>0 = Obeyes both correctly</td>
<td></td>
</tr>
<tr>
<td>(Open/close eyes, make fist/let go)</td>
<td>1 = Obeyes one correctly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Incorrect</td>
<td></td>
</tr>
<tr>
<td>2. Best Gaze</td>
<td>0 = Normal</td>
<td></td>
</tr>
<tr>
<td>(Eyes open - patient follows examiner’s finger or face)</td>
<td>1 = Partial gaze palsy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Forced deviation</td>
<td></td>
</tr>
<tr>
<td>3. Visual Fields</td>
<td>0 = No visual loss</td>
<td></td>
</tr>
<tr>
<td>(Introduce visual stimulus/threat to pt’s visual field quadrants)</td>
<td>1 = Partial Hemianopia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Complete Hemianopia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = Bilateral Hemianopia (Blind)</td>
<td></td>
</tr>
<tr>
<td>4. Facial Paresia</td>
<td>0 = Normal</td>
<td></td>
</tr>
<tr>
<td>(Show teeth, raise eyebrows and squeeze eyes shut)</td>
<td>1 = Minor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Partial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = Complete</td>
<td></td>
</tr>
<tr>
<td>5a. Motor Arm - Left</td>
<td>0 = No drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = Drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Can’t resist gravity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = No effort against gravity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = No movement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X = Untestable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Joint fusion or limb amp)</td>
<td></td>
</tr>
<tr>
<td>5b. Motor Arm - Right</td>
<td>0 = No drift</td>
<td></td>
</tr>
<tr>
<td>(Elevate arm to 90° if patient is sitting, 45° if supine)</td>
<td>1 = Drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Can’t resist gravity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = No effort against gravity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = No movement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X = Untestable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Joint fusion or limb amp)</td>
<td></td>
</tr>
<tr>
<td>6a. Motor Leg - Left</td>
<td>0 = No drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = Drift</td>
<td></td>
</tr>
<tr>
<td>6b. Motor Leg - Right</td>
<td>0 = No drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = Drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median scores of NIHSS (left, right)</td>
<td>Increase of odds of NIHSS scoring if stroke at left brain</td>
</tr>
<tr>
<td>---</td>
<td>--------------------------------------</td>
<td>---------------------------------------------------------</td>
</tr>
<tr>
<td>1a.</td>
<td>Level of consciousness</td>
<td>0, 0</td>
</tr>
<tr>
<td>1b.</td>
<td>LOC Questions</td>
<td>1, 0</td>
</tr>
<tr>
<td>1c.</td>
<td>LOC Commands</td>
<td>0, 0</td>
</tr>
<tr>
<td>2.</td>
<td>Gaze</td>
<td>0, 0</td>
</tr>
<tr>
<td>3.</td>
<td>Visual</td>
<td>0, 0</td>
</tr>
<tr>
<td>4.</td>
<td>Facial palsy</td>
<td>2, 1</td>
</tr>
<tr>
<td>5a.</td>
<td>Motor arm, left</td>
<td>0, 2</td>
</tr>
<tr>
<td>5b.</td>
<td>Motor arm, right</td>
<td>2, 0</td>
</tr>
<tr>
<td>6a.</td>
<td>Motor leg, left</td>
<td>0, 1</td>
</tr>
<tr>
<td>6b.</td>
<td>Motor leg, right</td>
<td>1, 0</td>
</tr>
<tr>
<td>7.</td>
<td>Limb ataxia</td>
<td>0, 0</td>
</tr>
<tr>
<td>8.</td>
<td>Sensory</td>
<td>0, 1</td>
</tr>
<tr>
<td>9.</td>
<td>Language</td>
<td>2, 0</td>
</tr>
<tr>
<td>10.</td>
<td>Dysarthria</td>
<td>1, 1</td>
</tr>
<tr>
<td>11.</td>
<td>Extinction/inattention</td>
<td>0, 1</td>
</tr>
<tr>
<td>Total</td>
<td>10, 8</td>
<td>2.98 (P = 0.004)</td>
</tr>
</tbody>
</table>

NIHSS, National Institutes of Health
Lateralization
Language -left hemisphere

Wada test
LH versus RH stroke
95% of aphasia (language impairment) due to LH damage

Localization of function
specific parts of the brain perform specific functions
structure x does y

Equipotentiality
all parts of brain are equally competent to do y
Broca's aphasia (EXPRESSIVE)-- nonfluent aphasia, difficulty in word production/grammar

Wernicke's aphasia (RECEPTIVE) -- fluent aphasia, word salad (anomia), poor comprehension
Broca's aphasia with severe agrammatism
Broca’s Aphasia

- slow and halting speech
- struggle to get certain words out, such as the names of objects, places or people
- speech content stripped down to simple elements
- only contains basic nouns and verbs ("want drink")
- writing ability is often similarly affected

may be able to understand some spoken language, but have difficulty understanding grammar. They may be unable to tell the difference between, "Maureen slapped the naughty boy" and "the naughty boy slapped Maureen."
Wernicke's aphasia:
Answering interview questions
Wernicke’s Aphasia

speak fluently using long sentences,
speech lacks meaning and often includes nonsense words.

Same difficulty may also occur when they write.

They may have difficulty understanding what people say, and what written words mean.

They often don't realise that they have difficulty understanding, and don't know why people can't understand them.
Neural processes after stroke
Mechanisms of injury

Cells die from lack of glucose/oxygen
“Penumbra” exposed to waste products
Fluid accumulates (edema)
Glia dump glutamate
Over-excitation kills additional cells
Possible that cells turn on death genes (apoptosis)

Further afield (other problems)
Distant areas (connected to stroke area) depress activity = diaschisis
Need to engage these areas in days after stroke
Mechanisms of recovery

1. Little by way of replacing cells

2. Engage untapped power of existing mechanisms
   E.g., de-afferentation of limb causes loss of use of that limb. Not because lose control. If force use, animals/humans develop skills with them.

3. Regrow axons
   periphery - good with myelin tract
   In CNS – glia inhibit
Mechanisms of recovery

4. Resprouting -- NORMAL PROCESS
   neurotrophins $\rightarrow$ collateral sprouting
   lesion momentum

5. Denervation (or disuse) supersensitivity

6. Reorganize/rewire tissues
Mechanisms of recovery

Treatments
- tPA – tissue plasminogen activator
dissolves clots (3 h window only)
- hypothermia – prevents cell death in animals?
- antagonize glutamate – careful!!!!
- occupational therapy

Brain cooling after cardiac arrest
- w cooling 35% minimal disability 50% mortality
- without cooling 21% 67%

Doesn’t work in conscious patients
Meta-analysis – looking at multiple studies together
Does occupational therapy help?? YES for daily activities
The effect is about 1 point on this scale of daily activities – not huge

**The Barthel Index**

<table>
<thead>
<tr>
<th>Function</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowels</td>
<td>0 = incontinent (or needs to be given enemata)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = occasional accident (once/week)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = continent</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>0 = incontinent, or catheterized and unable to manage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = occasional accident (max. once per 24 hours)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = continent (for over 7 days)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grooming</td>
<td>0 = needs help with personal care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = independent face/hair/teeth/shaving (implements provided)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toilet use</td>
<td>0 = dependent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = needs some help, but can do something alone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = independent (on and off, dressing, wiping)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeding</td>
<td>0 = unable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = needs help cutting, spreading butter, etc.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = independent (food provided within reach)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfer</td>
<td>0 = unable – no sitting balance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = major help (one or two people, physical), can sit</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = minor help (verbal or physical)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = independent</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mobility</td>
<td>0 = immobile</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = wheelchair independent, including corners, etc.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = walks with help of one person (verbal or physical)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = independent (but may use any aid, e.g., stick)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dressing</td>
<td>0 = dependent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = needs help, but can do about half unaided</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = independent (including buttons, zips, laces, etc.)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stairs</td>
<td>0 = unable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = needs help (verbal, physical, carrying aid)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = independent up and down</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bathing</td>
<td>0 = dependent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = independent (or in shower)</td>
<td></td>
</tr>
<tr>
<td>Patient’s Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Score</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Collin et al., 1988)
For 100 people treated, 11 avoided “poor” outcome
Animal model of stroke
induce a stroke on one side to get motor symptoms
various walking tasks – on a grid, etc
measure paw use, foot fall errors etc

Drug L655, 708
antagonizes GABA-\(\text{A}\) receptor

Start 3 days after stroke
Sham = surgery but no stroke

Vehicle = Injection but no drug
Genetic manipulations

Gabra5-/− lacks α5-subunit of GABA\textsubscript{A} receptor

Gabrd-/− lacks δ-subunit of GABA\textsubscript{A} receptors

wild type = genetically normal mice
Self-test question

What statement best characterizes the effective use of GABA antagonists after stroke

A. They help prevent immediately loss of cells
B. They prevent cell death from excito-toxicity
C. They counter inhibition after stroke
D. They just produce a more active brain which is useful in any context
E. All of the above
Self-test question

Which stroke would most likely cause a person to produce rambling sentences that don’t make any sense

A. Left frontal
B. Left temporal
C. Right occipital
D. Right frontal
E. All are equally likely
Hydrocephalus
Normal ventricles

Enlarged ventricles

Modified from Iwoa Virtual Hospital
Figure 1. The contrast among a normal brain in a normal adult (left), the brain of a normal man with impressive hydrocephalus (Oliveira et al., unpublished data; middle), and an equally impressive hydrocephalus in a 54-year-old man with deep cognitive and motor impairment since childhood (right; Oliveira et al., unpublished data).
Cameron Mott video

Rasmussen’s Syndrome
http://www.youtube.com/watch?v=2MKNsI5CWoU
Rasmussen’s syndrome
epilepsy takes over one hemisphere of the brain
starts in childhood
remove the dysfunctional hemisphere

even removal of the left hemisphere allows language
in the remaining hemisphere

because the damage is progressive
the OK hemisphere is training itself
removal removes interference of the dysfunctional hemisphere

extraordinary abilities to recover function
Kid develops left hemisphere epilepsy at 5 y 6 m

fMRI at 6 y 10 mo: left hemisphere language dominance

Remove left hemisphere at 9 y: profound aphasia and alexia

Starts getting comprehension back quickly

fMRI at 10 y 6 mo: right hemisphere activation with language tasks
What about adults?

Rarely done – thought to have lost some plasticity

53 year old, suffered head injury at 5 y
Spreading epileptic activity from left to right hemisphere
Wada test language function from right hemisphere

After surgery – seizures largely eliminated
Immediate aphasia
Some recovery, but language worse than before
Self-test question

How soon must a stroke sufferer get to the ER for her to get an effective drug treatment?

A. 30 min
B. 3 h
C. 6 h
D. 1 day
E. 2 days
Reading: Section 7.1

Study Questions:

1. Define “receptive fields.” How are they assessed? From this and other lectures, give several examples from different senses. Include peripheral and cortical sites.

2. Give several examples of how an auditory perception is derived from physical aspects of pressure waves.
1. transduction

2. receptive fields

3. neural codes
   - labeled lines
   - across-fiber processing

4. hierarchical organization

5. maps/organization

6. active constructions
   - regulation of input
   - perceive things are not there

7. adaptation
Pressure waves
Pitch = Frequency
Loudness = Amplitude
Hearing - perception of pressure (sound) waves
Vestibular Sensation - perception of gravity, acceleration

Lateral line organ
Modification for Inner Ear, Vestibular Sense?
(c) The middle ear
Nerve to tensor tympani (from mandibular branch of trigeminal nerve)

Tensor tympani muscle
Malleus
Incus
Tympanic membrane (eardrum)
Facial nerve
Branch to stapedius muscle
Stapedius muscle
Oval window
Round window
Stapes
Tip link

K^+

Stereocilia

Stimulation opens trapdoor
Nerve fibers:
1. Afferent, to cochlear nucleus of brain stem
2. Efferent, from lateral superior olivary nucleus
3. Afferent, to cochlear nucleus
4. Efferent, from medial superior olivary nucleus
How a cochlear implant works:

1. External speech processor captures sound and converts it into digital signals

2. Processor sends digital signals to internal implant

3. Internal implant converts signals into electrical energy, sending it to an electrode array inside the cochlea

4. Electrodes stimulate hearing nerve, bypassing damaged hair cells, and the brain perceives signals; you hear sound
Receptive fields of hair cells in basilar membrane
V-shaped tuning functions
Tonotopic organization
Low freq together
High freq together
Auditory Localization
Multiple mechanisms - need 2 ears to do well

1. Intensity differences
   head shadow
   sound is on side where intensity is greater
   high frequencies (>2000 Hz)

2. Arrival time
   at low frequencies, intensity is same
   takes longer to get to one ear
   brain calculates difference
   best studied in owls, bats
   midbrain/brainstem

Interaural Time Differences (ITDs)
Central nuc
External nuc
Optic tectum
A  Best ITD (μsec)

Topographic mapping
Shift of Auditory Tuning
After 8 Weeks of Experience
Critical period for this plasticity
Summary

1. Auditory processing occurs at several “levels”

2. Active processing of the system from “above”

3. Model systems teach us about how function emerges from function of specific neurons