What’s New in Neuroscience?
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Learning Objectives

- Apply new research on neural connectomes to differential diagnosis of disorders of language, cognition and motor planning.
- Develop comprehensive treatment plans based on neuroscience principles that drive maximal neuroplastic change.
- Utilize new neuroplasticity research to develop evidence-based goals and methodology for rehabilitation of language, cognition and motor planning.

Agenda

- New neurophysiology research on connectomes and their relevance to clinical practice in neurorehabilitation
  - language
  - attention
  - memory, and
  - executive functions
- New research neuroconnectomes upregulated during language, cognition and motor planning that drive neuroplasticity:
  - Acetylcholine – clinical methodology that drives arousal setting the brain up to reorganize
  - Facilitating selective attention
- Neuroexcitatory – clinical methodology that drives excitability of neural pathways for memory, attention and new connections
  - The neuromodulator equivalent of an adrenaline rush
  - The power of novelty in treatment
- Common drugs used for neuromodulation enhancement
- Dopamine – and the reward network
  - The reward network in adolescents versus adults
  - The importance and value of timely reward in clinical practice

Questions and answers

Selected References


Selected References (continued)

- Caeyenberghs, K. et al. (2012) Graph Analysis of Functional Brain Networks for Cognitive Control of Action in TBI. Brain April 1, 1293-1307
Selected References (continued)

• Nature Reviews Neuroscience. www.nature.com/reviews
• Schacter, D. et al. The Future of Memory, Remembering, Imagining, and the Brain. Neuron, 76 (4) 677-694

Reference Source for Chemistry and Rehabilitation aspects of neuroplasticity

• Neuron (2012) 76(1) Reviews on Neuromodulatory Mechanisms
• Chen, A. et al. (2011) Training of goal-directed attention regulation enhances control over neural processing for individuals with brain injury. Brain 134, 1541–1554
• Kim, Y H et al. (2009) Plasticity of the Attentional Network after Brain Injury and Cognitive Rehabilitation. Neurorehabilitation and Neural Repair (23) 488-497

Reference Access

• To get access to any of the articles in the reference list or referred to during the presentation or to purchase books in the reference list.
• Go to Google Scholar (not Google)
  – Type in the first author’s last name and a few major words from the article or topic of interest.
  Eg. Galaburda dyslexia genes
  – You can purchase the article through Science Direct (link on the left) or go to right links if available and download at no cost from the funding agency or supporting research center.

Let’s Start from the Beginning

Selected References (continued)

Progressed to Network Theory

- Network theory was an expansion of connectionistic theory that:
  - Was proposed after early neuroimaging results (PET and MEG scanning) revealed that distributed cortical regions fire in parallel and simultaneously during standard cognitive tasks like language processing.
  - Based on Hebbian stance that – neurons that fire together wire together.

New Technologies Expand Understanding Diffusion Tensor Imaging

- Measures diffusion (motion) of protons in water molecules.
- The linear structure of fiber tracts constrains proton diffusion and produces **anisotropy**.
- Provides clearly defined images of white matter tracts.

Tracts mature at different rates

**Lebel et al., 2008**
Cortical module mapping also progresses

- Typical brain function
- Disorders
Turken and Dronkers (2011) motor speech planning, fluency and grammar pathways

Turken and Dronkers (2011) – White Matter tracts underlying auditory speech processing

Combined methodologies yield insight into therapeutic processes

- gallantlab.org/semanticmovies/ - This is a great interactive site where you can manipulate the information on semantic space


Comparison of group semantic space across subjects
Potential treatment applications

• Better understanding of how the brain is organized for different types of cognitive processing
  – Hierarchically – as in semantic organization which supports research showing that semantic categories provide an effective way to treat word recall.
  – Economically – understanding connections that underlie working memory for example may help determine which cognitive tasks to select to underlie processing efficiency.

Clinical Takeaways

• Most neurological disorders may best be understood by a combination of modular and connection maps (connectomes).
• Differential diagnosis may be much easier once the connectome differences are corroborated – see issues with DSM-5 NYTimes, May 7, 2013.
• Treatment hierarchies can be developed using information from these combined constructs.
• Some developmental disorders of connectome organization and progressive dementias may be partially preventable or amenable to cognitive interventions that enable more efficient brain processing.

Understanding the Default Mode Network

So what is the Default Mode Network (DMF)?

“Two views of brain function”


Figure 2. Performance of a wide variety of tasks has called attention to a group of brain areas (a) that decrease their activity during task performance compared to resting state measurements (b) taken from [32]. These areas are often referred to as the brain’s DMN [32]. If one records the spontaneous BOLD fMRI signal activity in these areas in the resting state (arrows, a) what emerges is a remarkable similarity in the behavior of the signals between areas (b), a phenomenon originally described in the somatomotor cortex [147] and later in the DMN by Greicius and colleagues [38]. Using these fluctuations to analyze the network as a whole reveals a level of functional organization (c) that parallels that seen in the task-related activity decreases (a). Raichle, 2010
Bonnelle et al (2011) The greater the Selective Attention impairment the greater the DMN activity

Which takes us to Connectomes

- How do these modular systems integrate through the white matter fiber tracts for brain efficiency and plasticity

FROM THE JANUARY-FEBRUARY 2013 ISSUE of Discover Magazine:

New Project Maps the Wiring of the Mind
Project to trace all the brain’s main neural pathways begins its first human imaging.

By Kat McGowan | Wednesday, January 23, 2013
So where is this taking us clinically?

- Understanding long term consequences of acquired neuropathology in terms of atrophy of fiber tracts will allow us to prioritize processing systems to stimulate – For example, Irimia, et al, 2012.
- Understanding developmental and degenerative disorders in terms of neurophysiological patterns of disturbance rather than symptoms – For example - Bullmore and Sporns, 2012.
- Understanding attentional and memory processes and effective interventions – For example, Buckholtz and Meyer-Lindenthal (2012).

Default Mode Network and Connectome Research Applications

- Cognitive processing networks
- Developmental neuropathologies
  - Autism
  - Schizophrenia
With application to understanding disorders like Schizophrenia and Autism

Attentional Networks (Connectomes)

- Attention as a core component of cognitive control – deficits as distractibility and impulsivity
  - Wide distributed networks with frontal lobe providing top-down control.
  - Two primary attentional networks:
    - Frontal parietal – ignoring distractions and working memory.
    - Frontal striatal – lack of flexibility and impulsivity.
  - Sustained Attention predicted by the Default Mode Network.

Extended view

- Attention as a core component of Cognitive Control.

Inhibition/distractibility

- Holding information in mind while inhibiting a prepotent response
  - Day-night
  - Tapping (When I tap once you tap twice)
  - Appearance-reality (clouds)


Schacter et al. (2012) Visual spatial versus autobiographical planning and the default network

Response inhibition – Stroop-like test

RED GREEN BLUE YELLOW PINK
ORANGE BLUE GREEN BLUE WHITE
GREEN YELLOW ORANGE BLUE WHITE
BROWN RED BLUE YELLOW GREEN
PINK YELLOW GREEN BLUE RED

Chen et al, 2011

• Used computerized goal-directed attention regulation task.
  - 12 patients with chronic acquired brain injury.
  - Randomized to receive either the goals training intervention or education during the first 5-week study period.
  - The participants then switched over to the alternative condition for the second 5-week study period.
  - Of the 12 participants, five started with goals training and seven started with education. Behavioural and

Neural mechanisms of selective auditory attention are enhanced by computerized training:

Electrophysiological evidence from language-impaired and typically developing children

ERP attention effect for the FFW-LI, FFW-TD, and NoTx control groups, separately for pre- and post-testing
Interactive therapeutic activities for working memory training
See esp. Jaeggi, et al., Proceedings of the National Academy of Sciences
May, 2008.

Improving fluid intelligence with training on working memory
Susanne M. Jaeggi, Martin Buschkuehl, John Jonides, and Walter J. Perrig

Studies with normal adults

Working memory training improves reading processes in typically developing children.
Sandra V. Loessler Martin Buschkuehl Walter J. Perrig Susanne M. Jaeggi Volume 18 Issue 3 2012
Task Switching

- Card sorting
- Go/no-go (Simon says)
  - Can increase complexity to increase task switching


Maximizing Neuroplastic Change through what you do in therapy

- New principals and guidelines derived from neuroscience research help in selection of tasks
- Maximizing neuromodulation of neuroplasticity helps in selecting methodology
  - New research
  - Clinical takeaways

1. Balance Brain Stimulation

Chapman (2013)

- Active mental stimulation is required to improve or recover lost cognitive functions
- 80% rule (Merzenich & Jenkins)
  - Too low challenge creates boredom
  - Too high challenge creates frustration agitation
- Tasks need to be ratcheted up a notch to constantly achieve brain wiring
“Zone of Proximal Development”

- New concepts/skills are maximally learnable/processed because
  - they should be just difficult enough to engage the client/patient
  - yet easy enough to maintain high spirits

2. Strengthen Strategic Attention
Chapman (2013)


- Keep background stimulation as low as possible
  - The brain has to work harder to process input while blocking out extraneous distractions
  - The processing impaired/injured brain tires faster when there are extraneous stimuli
- Therapist can gradually add distractions during tasks to build tolerance

3. Practice Integrated Reasoning
Chapman (2013)

Start with higher-order processing

- Build in working memory exercises for all levels of processing difficulties
- Continue on to higher level reasoning tasks such as analogies, problem solving, pattern analysis

4. & 5. Stay Informed and Modify Based on New Research
Chapman (2013)

Expect new breakthroughs each year in neuroscience of plasticity and rehabilitation – especially with new connectome research

Never let your client give up – the brain can rewire for the rest of our lives

Maximizing Plastic Change in Therapy by How You Do It!

Neurochemistry of Neuroplasticity - Explaining the “How of Therapy”

GrowingTogether 2013 Visionary Conference
Different dimensions of adult cortical plasticity are enabled by the behaviorally-context-dependent release of:

- acetylcholine (focused attention/reward) (Kilgard, Bao)
- dopamine (reward, novelty) (Bao)
- norepinephrine (novelty) (Bollinger)
- serotonin (Bollinger)
- et alia

In infants, exposure-based plasticity is relatively uniform. In older children, learning-induced changes are complexly "nuanced" by differences in behavioral context that result in the differential release of 6 or 7 modulatory neurotransmitters.

Take away from Picciotto, Higley and Mineur (2012)

- ACh is an arousal neuromodulator
  - both excitatory and inhibitory
  - it enhances the salience of the primary signal and decreases attention to less important things going on in the environment
- To upregulate ACh in therapy—think TV commercials—(they are louder and grab you with color and quick relevance)
  - Put the client in charge of when information is presented ("signal [or tell me] when you are ready")
  - Use Movement and activity in the sessions to keep arousal high (why I wish I was an OT or PT), establish eye contact frequently with non-attending clients, use "bells and whistles"

Picciotto, Higley and Mineur (2012)

- ACh increases behaviors that are environmentaly adaptive
- ACh decreases responses to ongoing stimuli that don’t require immediate action

Sara and Bouret (2012)

- Norepinephrine [noradrenalin (NA)] regulates mood, motivation and arousal
- NA drives a reallocation of neural resources toward regions involved in attention, vigilant perception, and behavior control

Sara and Bouret (2012)

- Norepinephrine – the environmental adaptor chemical
  - A salient stimulus release of noradrenaline in its numerous target regions (blue arrows), including cerebral cortices, limbic structures, thalamus, cerebellum, brainstem, and spinal cord.
  - Surge of NA facilitates sensory and motor processing—reorganizing distributed functional networks & promoting behavioral adaptation.
Take away from Sara and Bouret (2012)

- Making content of sessions “emotionally relevant” is the key to increased norepinephrine.
  - The “ah hah” moment.
  - The “wow that is cool” response to information.
- Similar dopamine (coming up) – novelty works well.
  - Try presenting the information several different ways.
  - This is where the creativity of a clinician and engaging materials really come into play.

Take away from Tritsch and Sabitini (2012) Continued

- REWARD, REWARD, REWARD
  - Reward meaningfully and frequently
    - Know what is and is not rewarding for each person you work with.
    - Provide good personal examples of why and how that session applies to real situations.
    - Be careful about rewards (saying the same thing every time, like “nice try” or “good” is not rewarding.

Dopaminergic Modulation of Synaptic Transmission in Cortex and Striatum
Nicolas X. Tritsch and Bernardo L. Sabatini

Neuron 76, October 4, 2012

Take Away from Tritsch and Sabitini (2012) Continued

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Lesch and Waider (2012)

- Serotonin in the Modulation of Neural Plasticity and Networks: Implications for Neurodevelopmental Disorders. Neuron, 76, October 4, 2012
- Serotonin (5-HT) shapes brain development influencing social cognition and emotional learning.
- 5-HT and brain development are highly affected by genetics and environmental influences.

Take Away from Lesch and Waider (2012) and Kravitz et al (2012)

- The environment of the clinic should be safe and non-threatening.
- The goal of discipline should be to reward correct responses – and keep materials at an appropriate level for 80% correct.
- Withholding reward is preferable to punishment (adverse outcomes) – this is very important with adolescents.

Tritsch and Sabitini (2012)

- The prefrontal cortex is the major cortical recipient of Dopaminergic inputs.
- Dopamine (DA) is believed to play a critical role in several cognitive processes conducted by Pre Frontal Cortex networks, including
  - working memory,
  - attention, and
  - decision making.
Q & A