NIH Toolbox
Assessment of Neurological and Behavioral Function

"Toolbox Measures and Neurobiological Processes"

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NIH Blueprint

For more information, please visit www.nihtoolbox.org
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Toolbox Overview

- Four domains:
  1) Sensation (6 subdomains)
  2) Motor
  3) Cognition
  4) Emotion
- Where possible, use extant instruments; but, some new instruments may be developed or old ones extended
- Life span focus
- Goal: Adherence to the construct being measured

Was Toolbox development informed by neurobiological processes?

- Yes, to the extent possible.
- Sensory, motor domains: Relatively straightforward
- Cognitive domains: Targeted emphasis on measures with neuroimaging data and/or informative results from clinical populations to help validation
- Linkages between brain circuits and specific tasks
- Goal: Measure the full range of population-based performance

Cognitive Domain: Example (1)

- Zelazo & associates, executive function - cognitive flexibility
- Dimensional Change Card Sort (DCCS)
- Role of different areas of PFC in implementing increasingly complex rules
- Developed for toddlers & pre-school age children
- Quick, easy to administer
- Also being scaled up for older age levels

PFC Areas in Rule Development

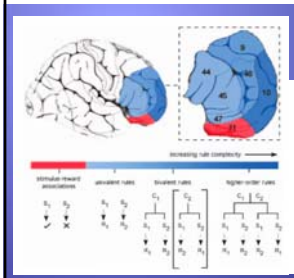


Fig. 1. A hierarchical model of rule representation in the lateral prefrontal cortex (PFC). A lateral view of the human brain is depicted at the top of the figure, with regions of the PFC identified by different Brodmann areas (BA): the orbitofrontal cortex (BA 11), the ventrolateral PFC (BA 44, 45, 47), the dorsolateral PFC (BA 9, 46), and the rostrolateral PFC (BA 10). Rule structures are shown below along a continuum from simple to complex, in colors corresponding to the brain regions that represent them. S = stimulus; check = reward; cross = nonreward; R = response; C = context, or task set. Brackets indicate a bivalent rule that is currently being ignored. The lateral PFC regions are shown in various shades of blue, with darker shades indicating regions that represent more complex rules. The orbitofrontal cortex is shown in red, to indicate that the rules represented in this region are qualitatively different from the types of rules represented in the lateral PFC, in that the rules provide information about the value of a stimulus. (Differences between the medial and the lateral orbitofrontal cortex with respect to the representation of rewards and punishments are not depicted here.)

Bunge & Zelazo, *Current Directions in Psychological Science*, 2006, 15, 118 - 121.

Cognitive Domain: Example (2)

- Bauer, Imitation-Based Assessment of Learning (IBAM)
- Developed for infants
- Developmental sensitivity
- Being scaled up for older age levels

Emotion Domain

- Emotion, mood, social cognition: Based on neurobiological processes to the extent possible given current knowledge
- So far, more difficult to tie to specific neural circuits
- Four sub-domains:
- – Negative Affect
- – Positive Affect
- – Stress and Coping
- – Social Relationships

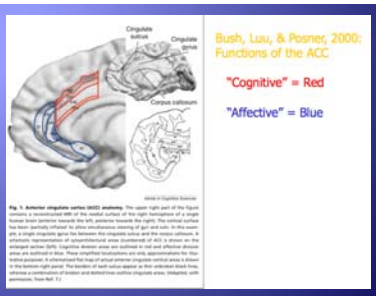
Modern Emotion Theory: Temperamental Predispositions

- Cf. modern temperament theories:
- – Negative Affect
- – Positive Affect
- – Constraint (or, disinhibition)
- These map well onto neurophysiological circuits, broadly speaking

Brain Circuits in Temperament

- Negative affect: Fear (amygdala); anxiety (bed n. stria terminalis, increased CRF receptor density)
- Positive affect: Mesolimbic dopamine system, possibly also oxytocin systems esp. for social behavior
- Constraint: Anterior cingulate, PFC

Constraint: "Cognitive" and "Affective" Components of ACC



Bush, Luu, & Posner, 2000: Functions of the ACC

"Cognitive" = Red

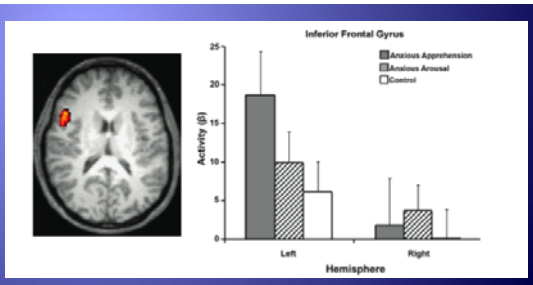
"Affective" = Blue

Bush, Luu, & Posner, *Trends in Cognitive Sciences*, 2000, *4*, 215 - 222

Emotions: New Construct Development

- Dimensional approaches (rather than discrete categories)
- Brain arousal/activation systems for aversive and for appetitive systems
- Brain measures have facilitated the validation of new constructs
- E.g., a new distinction of anxiety types:

Emotional Stroop: Anxious Apprehension.....



Engels, Heller, Mohanty, Herrington, Banich, Webb, & Miller, *Psychophysiology*, 2007, *44*, 355-364

Versus Anxious Arousal.....

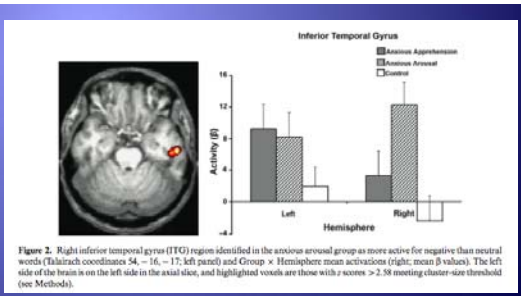


Figure 2. Right inferior temporal gyrus (ITG) region identified in the anxious arousal group as more active for negative than neutral words (Talairach coordinates 54, −16, −17; left panel) and Group × Hemisphere mean activations (right; mean β values). The left side of the brain is on the left side in the axial slice, and highlighted voxels are those with z scores > 2.58 meeting cluster-size threshold (see Methods).

Engels, Heller, Mohanty, Herrington, Banich, Webb, & Miller, *Psychophysiology*, 2007, 44, 352-363.

But, Common Hypoactivity in Anterior Cingulate

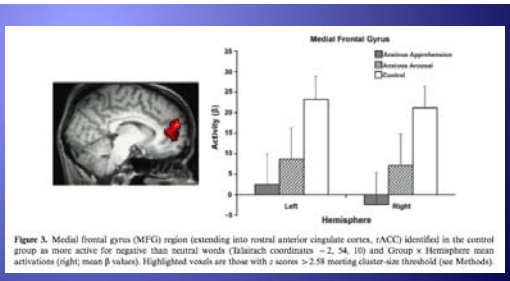


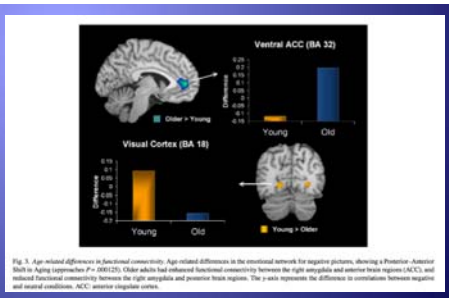
Figure 3. Medial frontal gyrus (MFG) region (extending into rostral anterior cingulate cortex, rACC) identified in the control group as more active for negative than neutral words (Talairach coordinates −2, 54, 10) and Group × Hemisphere mean activations (right; mean β values). Highlighted voxels are those with z scores > 2.58 meeting cluster-size threshold (see Methods).

Engels, Heller, Mohanty, Herrington, Banich, Webb, & Miller, *Psychophysiology*, 2007, 44, 352-363.

Emotion: Life Span Changes in Neurobiology

- Brain bases for previously noted changed changes in emotional response
- (1) Changes in phasic response to emotional stimuli
- (2) Persisting basal functioning changes – e.g, changes over time in levels of dopamine receptors

Response to Emotional Stimuli: Amygdala Connectivity in Young vs. Old



St. Jacques, Dolcos, & Cabeza, *Neurobiology of Aging*, in press (on-line).

Perspectives

- Cognitive functions are well advanced in linking to neurobiological circuits and processes
- Emotion is catching up
- Does this mean that all Toolbox measures must be, eventually, tightly linked to specific circuits to be viable?
- One opinion: No.

Behavior vs. Neurobiology (1)

- A key element in behavior is its flexibility: hierarchy and redundancy in interacting brain circuits
- Many behaviors seem to show plasticity that reflects dynamic activation of large areas of cortex, as opposed to specific circuits
- Two examples from aging:
- 1) "Cognitive reserve"
- 2) Recruitment of additional brain areas (often contralaterally) with age, to accomplish tasks

Behavior vs. Neurobiology (2)

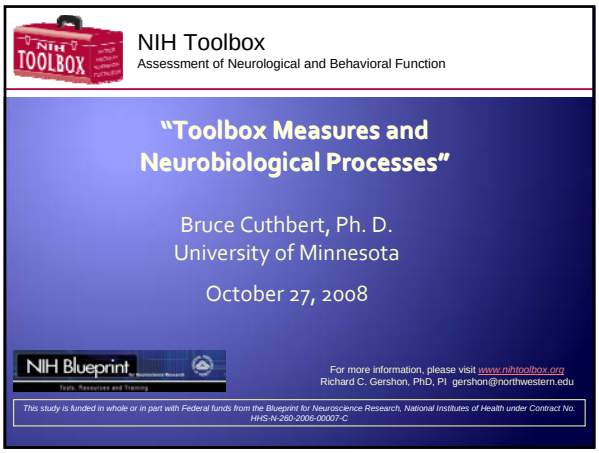
- The larger view: Behavior is the basis for natural selection processes in brain structure and function
- Therefore, it is necessary to study behavior in order to understand what the brain is doing
- Not simple 1:1 brain–behavior links, but behaviors that may reflect innumerable hormonal and neuronal, genetic and epigenetic (i.e., environmental) effects

Behavior vs. Neurobiology (2 - cont.)

- Some constructs, due to the brain's complexity, may remain very difficult to conceive in precise neurobiological terms but be very useful
- E.g., Life Satisfaction, Well-being:
- Might be: (1) High dopamine; (2) Low CRF; (3) High OXT; (4) High opioids; (5) High NPY; (6) Strong dorsal ACC; (7) Low sub-genual ACC [all, genetic & epigenetic] etc. etc. etc.
- May be invaluable summaries for brains doing well; cf. Tolstoy's happy and unhappy families

Neurobiology and the Toolbox's Future

- Nevertheless, understanding how the brain implements behavior will remain a major goal
- Stepwise advances in behavior and neurobiology: Advances in one domain drive advances in the other
- Toolbox: Epidemiological studies to generate new behavioral & neurobiological hypotheses
- Perhaps, these will occasion the need for future refinements to the Toolbox –
- Better measures of extant constructs, BUT also new constructs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