EXECUTIVE DYSFUNCTION IN BRAIN DISORDERS

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THE NEW EXECUTIVE BRAIN

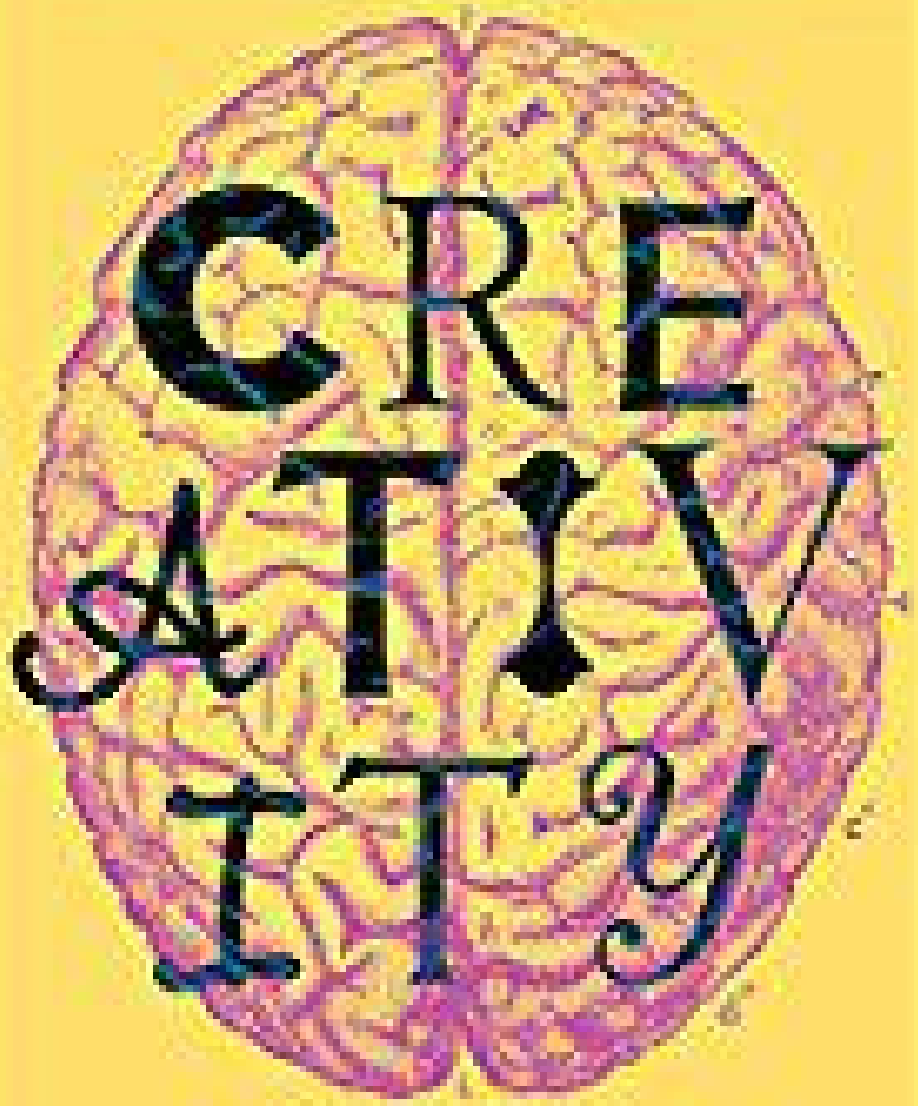
FRONTAL LOBES IN A COMPLEX WORLD

Elkhonon Goldberg, Ph.D.

OXFORD


Executive Functions
in Health and Disease
Elkhonon Goldberg

the human brain in the age of innovation



ELKHONON GOLDBERG, PhD

FRONTAL LOBE VULNERABILITY

Frontal lobes are particularly vulnerable across a wide range of disorders

- Hughlings Jackson’ s law of evolution and dissolution
- Extensive connectivity

DISORDERS CHARACTERIZED BY EXECUTIVE DEFICIT

- Cerebrovascular Disorders
- Schizophrenia
- Depression
- Bipolar disorder
- Tourette's/OCD
- Traumatic Brain Injury (TBI)
- Dementias (FTD, LB, AD)
- Parkinson's disease
- Huntington's disease
- Multiple sclerosis
- ADHD
- Non-verbal learning disability
- Autism

FRONTAL-LOBE ASYMMETRIES ACROSS MAMMALIAN SPECIES

- Yakovlevian torque – frontal poles (R>L)
- Frontal operculum (L>R)
- Spindle cells (R>L)
- NE (R>L)
- DA (L>R)
- Asymmetric gene expression

EXECUTIVE DEFICIT IN TRAUMATIC BRAIN INJURY

TBI STATISTICS FROM BRAIN TRAUMA FOUNDATION
www.braintrauma.org

- Traumatic Brain Injury (TBI) is the leading cause of death and disability in children and adults from ages 1 to 44.
- Every year, approximately 52,000 deaths occur from traumatic brain injury.
- Brain injuries are most often caused by motor vehicle crashes, sports injuries, or simple falls on the playground, at work or in the home.
- An estimated 1.5 million head injuries occur every year in the United States emergency rooms.
- At least 5.3 million Americans, 2% of the U.S. population, currently live with disabilities resulting from TBI.
- Males are about twice as likely as females to experience a TBI

TRAUMATIC BRAIN INJURY

-CLOSED

-OPEN (penetrating and perforating)

-BLAST

CAUSES OF TBI

-MVA
-FALLS
-JOB-RELATED
-ASSAULTS
-SPORTS
-MILITARY (BLAST)

EFFECTS OF TBI

-FOCAL EFFECTS:

COUP-CONTRECOUP

HEMATOMAS (SUBDURAL, EPIDURAL, INTRAPARENCHIMAL)

-DIFFUSE EFFECTS

DIFFUSE AXONAL INJURY

EDEMA

HYDROCEPHALUS

DELAYED EFFECTS OF TBI

-EDEMA

-EPIDURAL/SUBDURAL HEMATOMA

-HYDROCEPHALUS

-INFECTION/ABSCESS DUE TO SKULL FRACTURE

-SEIZURES

-WALLERIAN DEGENERATION

-DEMENTIA

PARTICULAR VULNERABILITY OF THE FRONTAL LOBES AND EXECUTIVE FUNCTIONS IN TBI

FRONTAL CONTUSIONS

“RETICULO-FRONTAL DISCONNECTION SYNDROME”
E. Goldberg et al, *Cortex*, 1989, 25:687-695

- **DIRECT ORBITOFRONTAL IMPACT**

ORBITOFRONTAL SYNDROME ("PSEUDOPSYCHOPATHIC")

-CAN BE DUE TBI, DEMENTIA, OR VASCULAR (AComA ANEURISM)

-POOR IMPULSE CONTROL

-AFFECTIVE LABILITY

-WITZELSUCHT

-INABILITY TO DELAY GRATIFICATION

-GENERAL DISINHIBITION

-AT RISK FOR ANTISOCIAL BEHAVIOR

Adrian Raine
THE ANATOMY OF VIOLENCE: THE BIOLOGICAL ROUTES OF CRIME, VINTAGE, 2014

ROTATIONAL and/or LINEAR ACCELERATION

DIFFUSE AXONAL INJURY

TBI AND MIDLINE STRUCTURES

Thalamus
Hypothalamo-pituitary axis
Septum
Corpus Callosum
Medial Forebrain Bundle

- **DIFFUSION TENSOR IMAGING (DTI)**

FRACTIONAL ANISOTROPY INDEX (0.0 – 1.0)

NO SIMPLE STRUCTURE-FUNCTION RELATIONSHIP IN TBI REPERCUSSIONS

-EFFECTS OF CORPUS CALLOSUM DAMAGE ARE OFTEN RELATIVELY BENIGN

-EFFECTS OF RETICULO-FRONTAL DAMAGE ARE OFTEN CATASTROPHIC

“RETICULO-FRONTAL DISCONNECTION SYNDROME”

E. Goldberg et al, *Cortex*, 1989, 25:687-695

SEVERITY OF TBI

	GCS	PTA	LOC
MILD	13-15	<1 day	0-30 min
MODERATE	9-12	1-7 days	30min-24hrs
SEVERE	3-8	>7 days	>24hrs

EPIDEMIOLOGY OF TBI SEVERITY

MILD TBI – 80%

MODERATE and SEVERE TBI – 20%

THE RIDDLE OF “MILD” TBI

-NEUROPSYCHOLOGICAL, RADIOLOGICAL EVALUATIONS OFTEN “UNREMARKABLE”

-LONG-LASTING “PERSONALITY” CHANGE AND FAILURE TO READAPT

-**PREMORBID PERSONALITY OR SUBTLE RETICULO-FRONTAL DISCONNECTION SYNDROME?**

ANOSOGNOSIA IN TBI

-COMMON CONSEQUENCE OF PREFRONTAL DYSFUNCTION

-COMPLICATES READAPTATION

-COMPLICATES REHABILITATION

EXECUTIVE DEFICIT AND FORENSIC ISSUES

- HISTORY OF TBI, FRONTAL-LOBE DAMAGE, AND CRIMINAL BEHAVIOR
- IQ INSENSITIVITY TO FRONTAL LOBE DYSFUNCTION
- KNOWING “RIGHT FROM WRONG” vs ABILITY TO ACT ON THIS KNOWLEDGE

EXECUTIVE DEFICIT IN DEMENTIAS

-ALZHEIMER’ S

-LEWY BODY

-FRONTOTEMPORAL

-KORSAKOFF’ S

-MULTIINFARCT

-MIXED

COMMON MISCONCEPTION: NO DEMENTIA WITHOUT MEMORY IMPAIRMENT

DSM-IV

Dementia defined as memory impairment plus least one of the following: aphasia, apraxia, agnosia or disturbance in executive functioning.

Making the presence of memory impairment a necessary condition for the diagnosis resulted was misleading and poorly informed.

It resulted in multiple “false negatives,” since could not account for typical presentations of LBD or FTD.

DSM-5

"Dementia" replaced by "Major Neurocognitive Disorder" defined as impairment of one or more of the following: memory, executive functions, language, complex attention, perceptual-motor, social cognition.

Sufficiently severe to interfere with everyday activities

Memory impairment no longer a necessary condition for the diagnosis.

Cognitive impairment in Alzheimer's disease

-**MEMORY:** BOTH ANTEROGRADE AND RETROGRADE AMNESIA

-**EXECUTIVE:** ASPONTANEITY, INDECISION, POOR PLANNING

-**LANGUAGE:** ANOMIA (BUT NO DYSARTHRIA)

-VISUO-SPATIAL

-**AROUSAL**

Executive deficit systematically underrecognized in Alzheimer's disease

-ANOSOGNOSIA IN PATIENTS

-MISDIAGNOSED AS DEPRESSION OR "PERSONALITY CHANGE"

-EXECUTIVE FUNCTION TESTS WEAK OR UNDERREPRESENTED IN NEUROPSYCHOLOGICAL ASSESSMENT BATTERIES

-PROBABLY UNDERREPRESENTED IN BRAIN BANKS, HENCE PREVALENCE UNDERESTIMATION

APPLICATIONS OF AGENT-CENTERED PARADIGM IN ALZHEIMER'S DISEASE

Common misdiagnosis of executive deficit in Alzheimer's disease

-DEPRESSION

-"LATE-ONSET SCHIZOPHRENIA"

-JUST MISSED – "PERSONALITY CHANGE"

Cognitive impairment in Lewy Body Disease

-MEMORY LESS AFFECTED

-COGNITIVE IMPAIRMENT OFTEN DOMINATED BY EXECUTIVE DEFICIT

-TREMOR

-VISUAL HALLUCINATIONS “PSYCHOSIS”

-WIDELY FLUCTUATING COGNITION AND AROUSAL

LBD and Parkinson's disease

-Substantia Nigra (and Ventral Tegmental Area ?) affected in both

-LBD if cognitive impairment first

-PD if tremors first

Differential diagnosis in LBD

-PARKINSON'S DISEASE

-DEPRESSION

-"LATE-ONSET SCHIZOPHRENIA"

hazards of neuroleptics in LBD ("neuroleptic malignant syndrome")

COMMON FAILURE TO RECOGNIZE EXECUTIVE DYSFUNCTION PRODROME IN LEWY BODY DEMENTIA

Parkinson's Disease

- Atrophy
  - Substantia Nigra (SN)
  - Ventral Tegmental Area (VTA)
- Motor impairment
  - Resting tremor
  - Bradykinesia
  - Parkinsonian facies

Cognitive Impairment in Parkinson's Disease

- Relationship to Lewy Body dementia
- Executive functions affected?

SN -> Striatum

VTA - > Prefrontal cortex

Hemiparkinsonian syndromes and lateralization of frontal lobe functions

“BALKANIZATION” OF CLINICAL NEUROSCIENCE – INEVITABLE BUT REGRETTABLE

CUTTING ACROSS TAXONOMIC BOUNDARIES

SYMPTOMATOLOGY OF FRONTAL-LOBE DAMAGE

PERSEVERATION – AN INABILITY TO SWITCH FROM ONE ACTIVITY TO THE NEXT

FIELD DEPENDENT DEBEHAVIOR – BEHAVIOR DOMINATED BY INCIDENTAL OUT-OF-CONTEXT STIMULI

CAN FRONTAL-LOBE PATHOLOGY PROVIDE INSIGHTS INTO HEMIPARKINSONIAN SYNDROMES?

COGNITIVE BIAS AND LATERALITY

- Left frontal damage – extreme context independence = perseveration
- Right frontal damage – extreme context dependence = field-dependent exploratory behavior

K. T. Hovik, M. Oie, E. Goldberg. Inside the Triple-Decker: Tourette's syndrome and cerebral hemispheres. In: E. Goldberg, ed. *Executive Functions in Health and Disease*, Academic Press, 2017

CBT IN HEMIPARKINSONIAN SYNDROMES

- Left hemi-PD like Right PFC lesions
- Right hemi-PD like Left PFC lesions

Huntington's Disease

-Genetic disorder characterized by autosomal dominant transmission

-50% likelihood of developing disease in affected individuals

-Particularly affects striatum

-Becomes symptomatic at 45-45 y.o.

-Motor symptoms: chorea

-Cognitive impairment: executive and other functions

-AMIOTROPIC LATERAL SCLEROSIS (ALS)

Brain regions particularly vulnerable in Frontotemporal Dementia

-Prefrontal (particularly left orbitofrontal)

-Temporal (particularly left anterotenmporal)

Cognitive impairment in FTD

-”BEHAVIOR VARIANT”: Executive deficit (particularly “orbitofrontal” disinhibition)

-”LANGUAGE VARIANT”: Language

-Visuospatial functions

COMMON FAILURE TO RECOGNIZE FTD AND DISMISS IT AS "PERSONALITY CHANGE"

Differential diagnosis in FTD

-OTHER DEMENTIAS

-”BIPOLAR DISORDER”

CUTTING ACROSS TAXONOMIC BOUNDARIES

SCHIZOPHRENIA AND FTD

- OF and AT: same normal lateralization (L>R)
- SCZ and FTD:OF more affected on L than R
- SCZ and FTD: AT more affected on L than R
- SCZ and FTD: high familial comorbidity, frequent diagnostic confusion

Asymmetric gene expression in normal and abnormal laterality

HYPOTHESIS: ABERRANT EXPRESSION OF THE SAME ASYMMETRICALLY EXPRESSED GENES PLAYS A ROLE IN SCZ (EARLY) AND FTD (LATE)

International Review of Psychiatry, April 2013; 25(2): 168–177

MICHAŁ HARCIAREK , DOLORES MALASPINA , TAO SUN & ELKHONON GOLDBERG

Schizophrenia and frontotemporal dementia: Shared causation?

KORSAKOFF'S SYNDROME

- Extreme alcohol abuse combined with nutritional deficiencies
- To be distinguished from non-Korsakovian alcohol induced syndrome

STRUCTURAL CHANGES IN KORSAKOFF'S SYNDROME

- Mammillary bodies
- Dorsomedial thalamus
- Brain stem (particularly around LC)
- Neocortex (particularly prefrontal)

COGNITIVE CHANGES IN KORSAKOFF'S SYNDROME

- Anterograde amnesia
- Retrograde amnesia
- Executive deficit
- Confabulation
- Anosognosia

MILD COGNITIVE IMPAIRMENT (MCI)

FROM MILD COGNITIVE IMPAIRMENT (MCI)

TO MILD NEUROCOGNITIVE IMPAIRMENT (mNCI)

ILLUSION OF CLASSIFICATIONS: DIFFERENT SUBTYPES ARE NOT TRULY DISCRETE

EARLY DIAGNOSIS OF PRODROMAL AND PRE-PRODROMAL STAGES

- Mild Neurocognitive Impairment (mNCI)
- “Pre-mNCI”
- Difficulties with identifying early executive deficit

CEREBROVASCULAR DISORDERS

-CEREBROVASCULAR ACCIDENT (CVA)

-TRANSIENT ISCHEMIC ATTACK (TIA)

-ANEURISMS

-ARTERIOVENOUS MALFORMATION (AVM)

EXECUTIVE DEFICIT IN CEREBROVASCULAR DISORDERS

- CVA is the most common cause of lateralized frontal damage

LATERALIZED AND GENDER DIFFERENCES IN FRONTAL LESION EFFECTS

Lateralization of emotional changes in CVA (Robert Robinson)

-LEFT FRONTAL CVA – QUASI-DEPRESSION

- PATHOLOGICAL CRYING

-RIGHT FRONTAL CVA – QUASI-EUPHORIA

- “BELLE INDIFFERENCE”

- PATHOLOGICAL LAUGHTER

Anterior Communicating Artery aneurism and orbitofrontal syndrome

DISEASES vs SYNDROMES

- Diseases are defined by causes
- Diseases are often discrete with clear boundaries
- Syndromes are defined as constellations of highly correlated symptoms
- Syndromes are often inherently dimensional, devoid of clear boundaries
- Therefore diagnoses are often subjective and arbitrary
- In clinical neuroscience this is further compounded by the fact that symptoms are determined by neuroanatomy more than by pathophysiology

EXECUTIVE DEFICIT IN NEUROPSYCHIATRIC DISORDERS

-SCHIZOPHRENIA

-AFFECTIVE DISORDERS (DEPRESSION, BIPOLAR)

-OBSESSIVE-COMPULSIVE DISORDER (OCD)

-TOURETTE’ S

KRAEPELIN ON *DEMENTIA PRAECOX* (1919)

...The frontal cortex...stands in close relationship to...higher intellectual abilities, and these are the functions which in our patients suffer profound loss. The manifold volitional and motor disorder... makes us think of finer disorder in the neighborhood of the precentral convolution. On the other hand, the peculiar speech disorder...and the auditory hallucinations ...probably point to the temporal lobe being involved.

NEUROIMAGING AND NEUROPATHOLOGICAL FINDINGS IN SCHIZOPHRENIA

- DIFFUSE SULCAR DILATION AND VENTRICULAR ENLARGEMENT: ABERRANT DEVELOPMENT OR ATROPHY?
- REDUCED OR INVERTED “YAKOVLEVIAN TORQUE”
- WIDESPREAD GLIOSIS,PARTICULARLY IN THE FRONTAL LOBES: POST-INFLAMMATORY?
- PHYSIOLOGICAL “HYPOFRONTALITY: PET

ONSET OF SCHIZOPHRENIA

-FIRST OVERT SYMPTOMS IN LATE TEENS/MID-20'S

– when prefrontal cortex normally matures

-INCREASINGLY CLEAR THAT NEURODEVELOPMENTAL PROCESS ABERRANT FROM VERY BEGINNING. WELL BEFORE THE FIRST BREAK

NEGATIVE AND POSITIVE SYMPTOMS OF SCHIZOPHRENIA

NEGATIVE:

- Avolition (dorsolateral?)
- Affective flatness (dorsolateral?)
- Cognitive impairment

POSITIVE:

- Hallucinations
- Delusions
- Paranoid ideation

COGNITIVE FINDINGS IN SCHIZOPHRENIA – ESSENTIALLY NEURODEVELOPMENTAL!

- EXTENSIVE COGNITIVE DEFICIT
- EXECUTIVE FUNCTIONS OF THE FRONTAL LOBES PARTICULARLY AFFECTED
- LANGUAGE IMPAIRMENT, OR IS THERE?
- DEVELOPMENTAL “ASSOCIATIE AGNOSIA”?
- ABERRANT TOP-DOWN COGNITIVE CONTROL:
  LANGUAGE > PERCEPTION
  PERCEPTION > SENSORIUM

DOPAMINE PATHWAYS AND POSITIVE SYMPTOMS IN SCHIZOPHRENIA

- MESOLIMBIC DA PATHWAY (L>R), LEFT TEMPORAL LOBE, AND AUDITORY HALLUCINATIONS
- MESOLIMBIC DA PATHWAYS, AMYGDALA, AND AFFECTIVE TONE
- MESOCORTICAL DA PATHWAY AND SOURCE MISIDENTIFICATION

NEUROLEPTICS: THERAPEUTIC AND IATROGENIC EFFECTS IN SCHIZOPHRENIA

- THERAPEUTIC EFFECTS ON POSITIVE SYMPTOMS: MESOLIMBIC DA, MESOCORTICAL DA EFFECT, OR BOTH?

  PROBABLY MOSTLY MESOLIMBIC

- IATORGENIC EFFECTS:

  TARDIVE DYSKINESIA: NIGROSTRIATAL EFFECT

  "TARDIVE DYSMENTIA" AND "AKYNESIA": MESOCORTICAL EFFECTS?

DEPRESSION

- Low 5-HT and NE
- Enlarged sulci/ventricles
- Physiological “hypofrontality”
- Cognitive impairment dominated by executive and “right-hemispheric” findings
- Cognitive-emotional uncoupling following treatment

TREATMENT OF DEPRESSION

- Pharmacology:

  SSRI's – 5HT or neurogenesis?
- Electroconvulsive therapy - ECT
- Transcortical magnetic stimulation – TMS – applied to prefrontal regions
- Psychotherapy

DIFFERENTIAL DIAGNOSIS IN DEPRESSION

- "Late-onset" depression vs Dementia with frontal-lobe onset
- "Personality" change secondary to frontal damage in TBI
- Left frontal CVA

"PSYCHOSURGERY" – SURGICALLY INDUCED FRONTAL SYNDROMES

- FRONTAL LEUCOTOMY/LOBOTOMY
  - Egas Moniz
  - Walter Freeman
- CINGULOTOMY

NEURODEVELOPMENTAL DISORDERS

ATTENTION DEFICIT (HYPERACTIVITY) DISORDER

ATTENTION, EXECUTIVE FUNCTIONS, AND AROUSAL SYSTEMS

COMPONENTS OF THE AROUSAL SYSTEM

- Ventral brainstem arousal core
- Fronto-mesencephalic component: Voluntary attention and AD(H)D
- Cortico-thalamic component: Automatic attention and hemineglect/ hemiinattention

AROUSAL IN ADHD: A FORM OF "RETICULO-FRONTAL DISCONNECTION SYNDROME"

E. Goldberg et al, *Cortex*, 1989, 25:687-695

ADHD vs. DYSEXECUTIVE SYNDROME

Executive deficit and inattention sometimes co-occur and sometimes don’t

ADHD OVERDIAGNOSIS

ADHD DIAGNOSIS IS OFTEN MADE CASUALLY AND IRRESPONSIBLY BY PEOPLE NOT QUALIFIED TO MAKE SUCH DIAGNOSES

ADHD HAS ACQUIRED A TABLOID STATUS

LUMPING UNDER THE ADHD LABEL ANY NUMBER OF HETEROGENEOUS CONDITIONS

ADHD IS OFTEN THE ONLY DIAGNOSIS WITH WHICH THE GENERAL PUBLIC IS FAMILIAR, THIS FURTHER CONTRIBUTING TO ITS INDISCRIMINATE USE

THE WORLD DIVIDED INTO HEALTHY PEOPLE AND PEOPLE WITH ADHD

AS A RESULT, PRIOR ADHD DIAGNOSIS CARRIES LITLE OR NO INFORMATION

ADHD EPIDEMIOLOGY

DSM-IV CRITERIA (USA): 6-7% OF CHILDREN, 2-5% OF ADULTS

ICD-10 CRITERIA (EUROPE): 1-2% OF CHILDREN

BOY:GIRL RATIO OF 3:1

DIAGNOSIS MORE COMMON IN NORTH AMERICA THAN IN ASIA, AFRICA

RATE OF DIAGNOSIS IN USA AND UK INCREASED SINCE 1970’S

ADHD “COMORBIDITIES”

ANXIETY DISORDER

CONDUCT DISORDER

BEHAVIORAL PROBLEMS

OBSESSIVE COMPULSIVE DISORDER

TIC DISORED

ADHD and TICS

TICS ARE PRESENT IN 27% OF CHILDREN DIAGNOSED WITH ADHD - COMPARED TO 8-9% IN GENERAL POPULATION (5-18% OF BOYS AND 1-11% OF GIRLS)

UP TO 64% OF CHILDREN DIAGNOSED WITH TOURETTE'S ARE ALSO DIAGNOSED WITH "COMORBID" ADHD

TICS REPORTED TO BE TRIGGERED BY STIMULANTS IN A SUBSET OF ADHD CHILDREN – POSSIBLY IN AS MANY AS 25%

Confusion between hyperactivity and excessive exploratory behavior

STANDARD DIAGNOSIS OF TOURETTE'S SYNDROME IS BASED ON THE PRESENCE OF

TICS - MOTOR AND VOCAL

British Medical Journal, 1992; 305: 1515-1516

Oliver W. Sacks

Tourette's syndrome and creativity

Duality of symptoms:

"stereotypic"

"phantasmagoric"

EXCESSIVE EXPLORATORY BEHAVIOR

"Stimulus bound behavior"

"Utilization behavior" – Francois Lhermitte

"Field-dependent behavior" – Alexandr Luria

Echo behaviors (echolalia, echopraxia)

TOURETTE’ S SYNDROME:

STANDARD DEFINITIONS OF TOURETTE’S ENCOMPASS ONLY HALF OF SYMPTOMATOLOGY - TICS

EXPLORATORY BEHAVIORS ARE NOT RECOGNIZED AS PART OF TOURETTE’S OR AS A DISTINCT ENTITY (e.g. NO SCALES)

THEY ARE CONFLATED WITH HYPERACTIVITY

TOURETTE'S SYNDROME:

TICS AND EXPLORATORY BEHAVIORS

TICS ARE PERSEVERATIONS

EXPLORATORY BEHAVIORS ARE CONFLATED WITH HYPERACTIVITY

“BALKANIZATION” OF CLINICAL NEUROSCIENCE – INEVITABLE BUT REGRETTABLE

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SYMPTOMATOLOGY OF FRONTAL-LOBE DAMAGE

PERSEVERATION – AN INABILITY TO SWITCH FROM ONE ACTIVITY TO THE NEXT

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CAN FRONTAL-LOBE PATHOLOGY PROVIDE INSIGHTS INTO ADHD AND TOURETTE'S ?

COGNITIVE BIAS AND LATERALITY

- Left frontal damage – extreme context independence = perseveration
- Right frontal damage – extreme context dependence = field-dependent exploratory behavior

“HEMI-TOURETTE’S” :

LEFT FRONTO-STRIATAL DYSFUNCTION ->TICS ?

RIGHT FRONTO-STRIATAL DYSFUNCTION -> EXPLORATORY BEHAVIORS MISDIAGNOSED AS HYPERACTIVITY ?

IS THE DIAGNOSIS OF "TS COMORBID WITH ADHD" OFTEN A MISDIAGNOSIS, AN ARTIFACT OF OVERLY NARROW DIAGNOSTIC CRITERIA FOR TS?

HYPOTHESIS:
WHAT WE CALL “TS” IS IN FACT RIGHT HEMI-TS, WHEREAS LEFT HEMI-TS IS MISDIAGNOSED AS SOMETHING ELSE, OFTEN AS ADHD

OSLO TS SAMPLE (K. Hovik et al)

16 right-handed boys (9-17 y.o.)

Right hemi-TS defined as the right hand slower than the left hand

Left hemi-TS defined as the left hand slower than the right hand by more than 1.5 sd

et al)

COGNITIVE TESTS AND CLINICAL SCALES

“ Right hemi-TS” (left fronto-striatal dysfunction): Focus/Sustained Attention Impairment + Depression

“ Left hemi-TS” (right fronto-striatal dysfunction): Hyperactivity/Impulsivity + Anxiety

OSLO TS SAMPLE (K. Hovik et al)

CLINICAL DIAGNOSIS

“ Right hemi-TS” (left fronto-striatal dysfunction): TS

“ Left hemi-TS” (right fronto-striatal dysfunction): TS+ADHD/ASD

“ Symmetric TS” : equal breakdown between TS and TS+

CLINICAL DIAGNOSIS BY TS SUBTYPE

Clinical Diagnosis	TS	TS+
Left hemi-TS (N=4)	0	4
Right hemi-TS (N=5)	4	1
Symmetric TS (N=7)	4	3

While the samples are admittedly small, the interaction between the clinical diagnosis of TS versus TS+ and the “hemi” designation is significant (Fisher Exact Probabilities Test, p=.04762).


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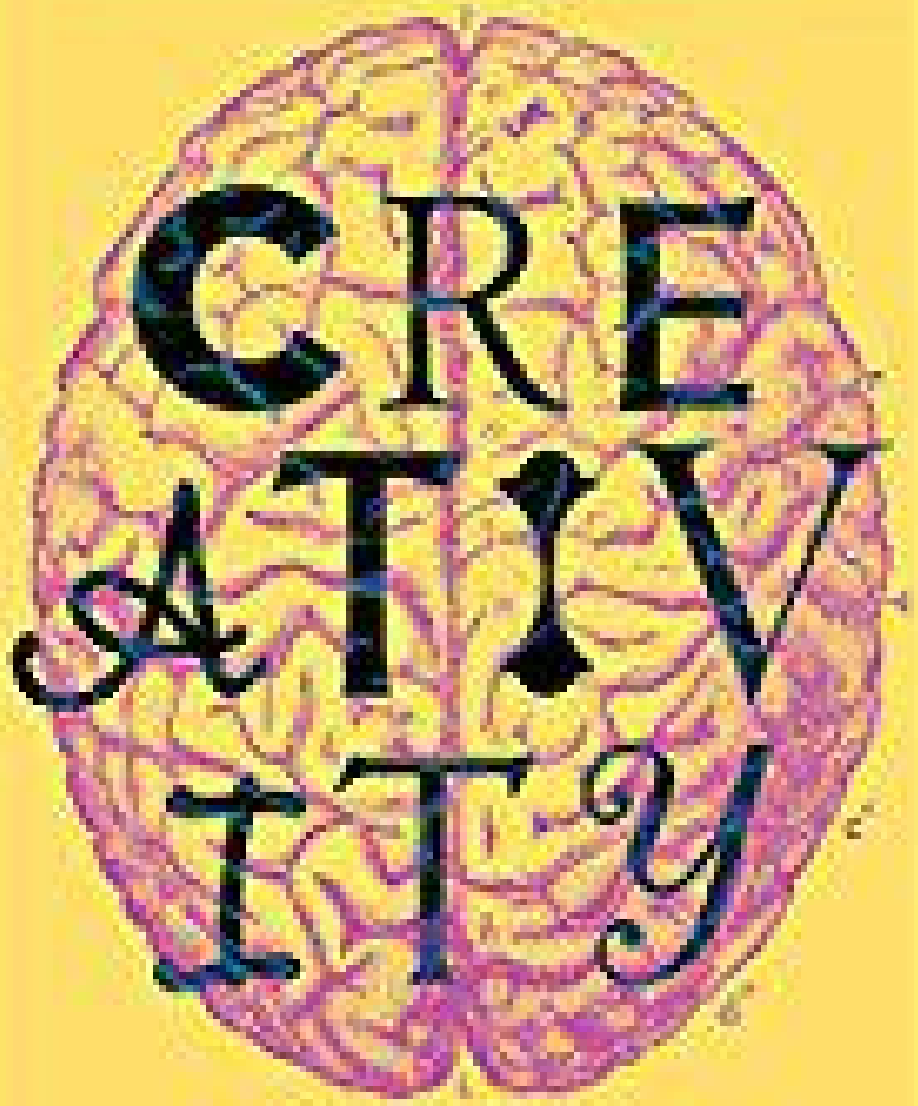
the human brain in the age of innovation



ELKHONON GOLDBERG, PhD

AUTISM SPECTRUM DISORDER (ASD) SUBSUMES:

- AUTISM
- CHILDHOOD DISINTEGRATIVE DISORDER
- PERVASIVE DEVELOPMENTAL DISORDER - NOS
- ASPERGER (AND ITS RELATIONSHIP TO NVLD)
- REMOVES THE ENDLESS, IDLE DIAGNOSTIC DEBATES

EPIDEMIOLOGY OF AUTISM SPECTRUM DISORDER (ASD)

www.autismspeaks.org

- MORE COMMON IN BOYS THAN IN GIRLS (~4:1)
- MORE THAN 2 MILLION IN THE USA
- IN BOYS: 1/42
- IN GIRLS: 1/189
- TEN-FOLD INCREASE IN PREVALENCE IN 40 YEARS; 10-17% ANNUAL INCREASE IN RECENT YEARS:

  AUTHENTIC INCREASE OR CHANGE IN DIAGNOSTIC SENSITIVITY?

CAUSES AND RISK FACTORS OF AUTISM SPECTRUM DISORDER (ASD)

- SPECIFIC GENES AND/OR MUTATIONS

- INSUFFICIENT PRUNING

- CHILDHOOD-ONSET SEIZURE DISORDER (~30%)

- EXCESSIVELY HIGH TESTOSTERONE LEVELS
  (Simon Baron Cohen)

- MATERNAL/PATERNAL AGE

- PERINATAL HYPOXIA

- NO EVIDENCE TO SUPPORT THE ANTIVACCINATION HYPE

COGNITIVE FEATURES OF AUTISM SPECTRUM DISORDER (ASD)

- DIFFICULTIES WITH SOCIAL INTEGRATION
- PERSEVERATIVE BEHAVIOR AND INTERESTS
- COGNITIVE IMPAIRMENT, OFTEN IN THE VERBAL DOMAIN

ADDICTION

Role of DA pathways

Substance dependence

Behavioral addictions

ADDICTION

- SUBSTANCE DEPENDENCE
  - Alcohol
  - Nicotine
  - Opioid (e.g. Morphine, Heroin)
  - Sedatives (e.g. Barbiturates)
  - Cocaine
  - Cannabis
  - Aphetamine
  - Hallucinogens
  - Inhalants
  - etc

- BEHAVIORAL ADDICTION
- Most cases in young (18yo<) or older (>50yo)
- Acute systemic illness followed by chronic cognitive impairment
- Particular damage in the temporal lobes
- Cognitive impairment dominated by memory impairment
- Similar but milder syndromes linked to CMV, EB

ADDICTION

- **BEHAVIORAL ADDICTIONS**
  - **Gambling**
  - **Pornography ?**
  - **Video games ?**
  - **etc**