



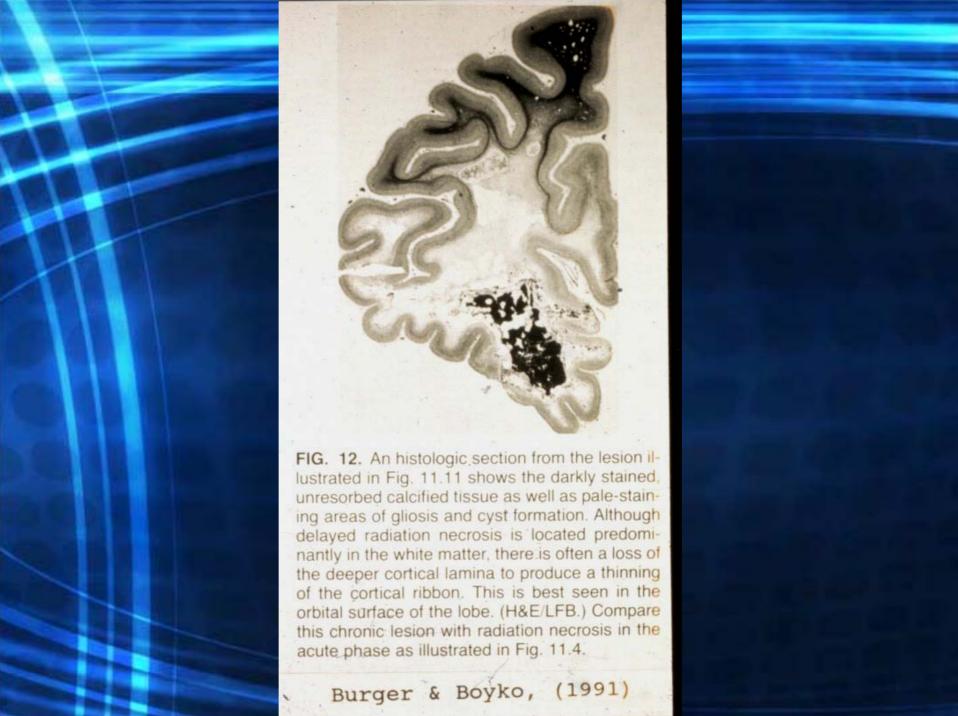
- Pediatric Brain Injuries
- Current Outpatient Standard of Care
- A Revised Treatment Standard
- Results of a Nation-wide Phase III Clinical Trial
- Where to Next?

# Oncology Brain tumors Leukemias (ALL)

# Neuropathology of Brain Irradiation

Demyelination
Gliosis
Vascular Necrosis
Focal Necrosis
Calcification

White Matter Disease



# Neuropathology of Intrathecal Methotrexate

Gliosis

Demyelination

Vascular Necrosis

White Matter Disease

# Effects of Brain Irradiation/MTX on Neuropsychological Functions

- Declines in intelligence
- Attention/concentration disturbances
- Reduced processing speed
- Memory problems
- Visual-spatial deficits
- Visual-motor integration problems
- Executive functions deficits
- Arithmetic difficulties



- Vigilance attention
- Reduced processing speed
- Working memory

#### **CNS Insult**

#### Neurological/Biological Factors

- Severity
- Pre-existing
- Genetics

#### **Developmental Factors**

- Age
- Gender
- Intelligence

#### **Time Since Onset**

- Acute
- Chronic
- Trajectory

#### **Mitigation**

- Rehabilitation
- Reserve capacity
- Family/Resources





- Functional reorganization proximal/distal
- Training facilitates biological repair
- Learning occurs

## Brain Injury Habilitation/Rehabilitation

Adult	Childhood
Established functions	Emerging/developing
Work	School
More mature	Less mature
coping/language	coping/language
Spontaneous recovery	Growth into deficits
Spouse/children	Caregivers/siblings
Less tolerance	More tolerance

# Drill Oriented Remediation (Physical Therapy Model)

- Tutorial/repetition
- Guided practice/assistance
  - Model
  - Prompt
  - Check
- Direct instruction
- Frequent review
- Independent work



- 504 Plan
- Individualized education plan
- Speech/language therapy services
- Occupational therapy services
- Special classroom
- Medication

#### **New Standard of Care**

Brief/Focused Outpatient Rehabilitation



**Educational Intervention** 



- Brain injury rehabilitation
- Educational psychology Special Education
- Clinical psychology (CBT)



- Individual
- Short term (4-5 months)
- 20 two-hour sessions (40 treatment hours)
- Team orientation
- Psychotherapy



- Practice drills (Alternating/50-80%)
- Mnemonic strategies
  - Visual imagery
  - Acronyms
  - Chunking

# Metacognitive Strategies

Preparation

On-Task

Post-Task



- Magic/special words
- Soup breath
- Game face
- World record
- Warm up my brain



- Talk to myself
- Mark my place
- Look for shortcuts
- Time out/start again
- Look at the floor



- Check my work
- Ask for feedback
- Reward myself
- Learn from my mistakes
- Try it again



- Cognitive-Behavioral interventions
- Psychotherapeutic environment
- Programmatic/Individualized

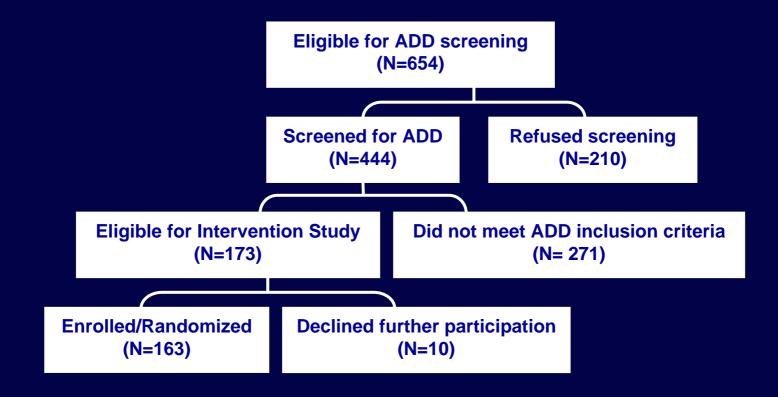
### A Multi-Center, Randomized Clinical Trial of a Cognitive Remediation Program for Childhood Survivors of a Pediatric Malignancy

Robert W. Butler, Oregon Health & Science University, Portland, OR Donna R. Copeland, UT/MD Anderson Cancer Center, Houston, TX Diane Fairclough, Colorado Health Sciences Center, Denver, CO Raymond K. Mulhern, St. Jude Children's Hospital, Memphis, TN Ernest Katz, Children's Hospital Los Angeles, Los Angeles, CA Anne E. Kazak, The Children's Hospital of Philadelphia, Philadelphia, PA Robert Knoll, Children's Hospital of Pittsburgh, Pittsburgh, PA Olle J. Sahler, University of Rochester Medical Center, Rochester, NY

# Participants (70-30)

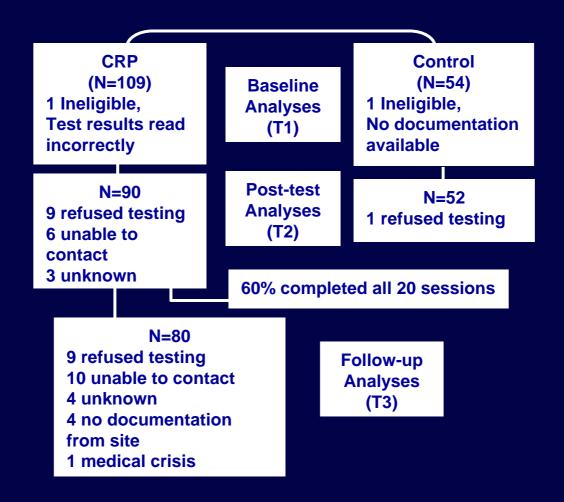
- 161 Pediatric cancer survivors (1 yr)
- Age 6-17
- 7 Nationwide sites
- No pre-diagnosis involvement
- Documented attentional disturbance
- IQ ≥ 50
- Intact language/sensorium

#### **Consort Flow**



N= 161 based on Immediate Declines

#### **Consort Flow**



# **Sample (n=161)**

Comparisons of Group Characteristics					
		Number of		Standard	
Characteristic	Group	Subjects	Mean	<b>Deviation</b>	<i>p</i> -value
Age	CRP	108	10.8	3.4	0.49
	Control	53	11.1	3.1	
Grade	CRP	103	5.0	3.3	0.26
	Control	53	5.6	3.3	
SES	CRP	99	3.2	1.0	0.99
	Control	49	3.2	1.1	
Age at DX	CRP	108	4.9	3.3	0.25
	Control	53	5.6	3.4	
Time since	CRP	108	<b>5.8</b>	2.8	0.60
DX	Control	53	5.6	3.2	
Male	CRP	67	n/a	n/a	n/a
	Control	37			

# Demographics

Race	p = 0.67	
American	CRP	2.8
Indian	Control	1.9
Asian	CRP	3.7
	<b>Control</b>	0.0
Black	CRP	10.2
	Control	11.5
Caucasian	CRP	63.9
	Control	67.3
Hispanic	CRP	17.6
	Control	19.2
Other	CRP	1.9
	Control	0.0

#### Cognitive/Behavioral Status At T1

CRP	107	89.2	15.9	0.10
Control	<b>52</b>	93.8	16.6	
CRP	107	92.0	16.3	0.48
Control	52	94.0	17.9	
CRP	107	88.5	15.6	0.02
Control	<b>52</b>	94.5	15.7	
CRP	106	71.6	16.2	0.77
Control	53			
				0.30
Control	53	59.5	16.5	
•				0.40
		<u> </u>		
		67.4		0.76
Control	51	66.8	12.9	
	CRP Control CRP Control CRP Control CRP Control CRP Control CRP	CRP 107 Control 52  CRP 107 Control 52  CRP 106 Control 53 CRP 106 Control 53  CRP 106 Control 51 CRP 106 Control 51 CRP 106	Control       52       93.8         CRP       107       92.0         Control       52       94.0         CRP       107       88.5         Control       52       94.5         CRP       106       71.6         Control       53       70.8         CRP       106       62.7         Control       53       59.5         CRP       106       68.9         Control       51       67.2         CRP       106       67.4	Control       52       93.8       16.6         CRP       107       92.0       16.3         Control       52       94.0       17.9         CRP       107       88.5       15.6         Control       52       94.5       15.7         CRP       106       71.6       16.2         Control       53       70.8       14.4         CRP       106       62.7       18.4         Control       53       59.5       16.5         CRP       106       68.9       11.2         Control       51       67.2       11.7         CRP       106       67.4       11.7         CRP       106       67.4       11.7

Indices (Alpha)	Measures (correlation with total)		
A: Academic Achievement (0.93)	WRAT-III		
	Reading	0.81	
	Spelling	0.79	
	Arithmetic	0.85	
	PIAT-R		
	Reading	0.74	
	W-J:R		
	Calculations	0.77	
	Applied Problems	0.82	
	WISC-III		
	Arithmetic	0.76	

Indices (Alpha)	Measures (correlation with total)		
B: Brief Focused Attention (0.72)	WISC-III		
	Digits forward	0.46	
	WRAML		
	Sentence Memory	0.70	
	CMS		
	Stories Immediate	0.46	
	RAVLT		
	Trial 1	0.44	

Indices (Alpha)	Measures (correlation with total)	
C: Working Memory (0.62)	WISC-III	
	Digits backward	0.45
	STROOP	
	Trial 3	0.30
	TRAILS	
	В	0.37
	BTA	
	Sum Score	0.51

Indices (Alpha)	Measures (correlation with total)		
D: Memory Recall (0.70)	CMS		
	Stories Delay	0.49	
	ROCF		
	Delay	0.48	
	<i>RAVLT</i>		
	Delay	0.56	
E: Vigilance (0.77)	CPT-II		
	Omissions	0.65	
	Hit RT	0.53	
	Variability	0.69	

# Statistical Significance (Interactions)

- A. Academic Achievement t=3.05, p=0.003, ES=0.53
- B. Brief Focused Attention t=0.15, p=0.9, ES=0.02
- C. Working Memory t=1.30, p=0.20 (Stroop p<0.05), ES=0.15
- D. Memory Recall t=-0.90, p=0.37, ES=-0.11
- E. Vigilance *t*=0.76, *p*=0.45, ES=0.10



- Parent Rating (Inattention)
- Teacher Rating (Inattention)
- Teacher Rating (ADHD)
- Self Report (CFSEI)

# Statistical Significance (Other/Self Report)

- 1. Parent Inattention *t*=-3.61, *p*<0.001, ES=-0.48
- 2. Teacher Inattention t=-1.00, p=0.32, ES=-0.21
- 3. Teacher ADHD t=-0.42, p=0.76, ES=-0.11
- 4. Total CFSEI t=0.76, p=0.45, ES=0.10

# Individual CRP Analyses

- Achievement T1-T3
- Focused Attention T1-T3
- Working Memory T1-T2
- Learning T1-T3
- Teacher Inattention T1-T2
- Self Esteem T1-T3

*p*≤0.05

## Compliance

- Gender/SES/Time Since Dx (N.S.)
- Older Age:

 $\downarrow$  T2 p=0.04

#### Conclusions

- CRP did have a significant effect on critical areas of functioning.
- Generalization occurred
- Effect sizes are modest
- Compliance is an issue
- Individual variables remain unclear

**But....** 

# Conditions Most Likely to Increase Effectiveness of Cognitive Remediation

- Team approach/knowledge
- Increased compliance
- High functioning family/decreased family stress
- Promotion of generalization

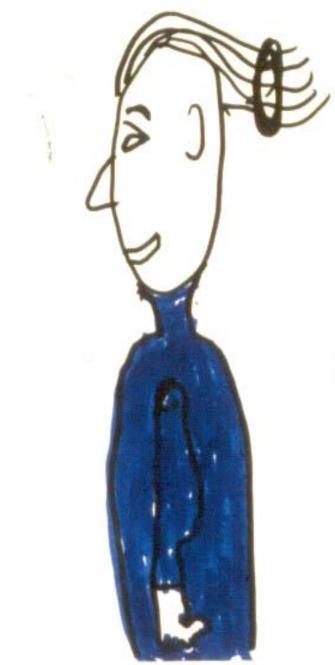
#### **Second Generation CRP**

- Problem Solving Skills Training (6-8 sessions)
  - Increase treatment compliance
  - Educate caregivers about education system
  - Reduce family chaos

#### **Second Generation CRP**

- Ecological intervention
  - Sleep
  - Nutrition
  - Exercise
- School interventions

**-?** 



This proofans makes me feel happy.

Travis

