Inter-relationships Between Post-TBI Sequelae

Northern CA TBI Model System of Care
Santa Clara Valley Medical Center
www.tbi-sci.org

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Common Sequelae after TBI

- Depression
- Sleep disorders/disturbances
- Decreased/ Increased Level of activity
- Pain
- Use of Medications
- Substance use/abuse
- Fatigue

Definition of Fatigue

- "the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity"

  Aaronson et al, 1999

Fatigue after TBI

- Prevalence rates
  - 50%-80% in people with TBI
  - 10%-28% in people without disability

One of the most common sequelae after TBI

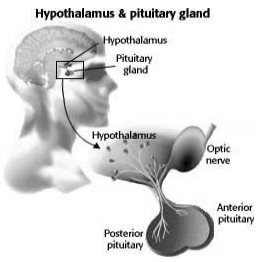
Fatigue after TBI

- Fatigue doesn't go away
  - In a sample of individuals with TBI living in the community
    - 68% reported fatigue 2 years post-injury
    - 73% reported fatigue 5 years post-injury

Possible Contributing Factor

- Hypopituitarism
  - non-specific symptoms of pervasive fatigue, decreases in strength, poor sense of well-being overlap with those after TBI
  - In particular, the syndrome of growth hormone (GH) deficiency, gonadal, adrenal, and thyroid dysfunction

Why the Pituitary?



Hypopituitarism after TBI

	Abnormal Level/Stimulation			
	GH	Cortisol	GT	Thyroid
6-36 mnths post Agha et al, 2004	11% (11/102)	13% (13/102)	12% (12/102)	1% (1/102)
1-5.3yrs Bondanelli et al, 2004	28% (14/50)	0% (0/50)	14% (7/50)	10% (5/50)
1 year post Agha et al, 2005	10% (5/48)	19% (9/48)	12% (6/48)	2% (1/48)
1 year post Tanriverdi et al, 2006	33% (17/51)	20% (10/51)	8% (4/51)	6% (3/51)
1 year post Klose et al, 2007	29% (11/58)	3% (2/58)	2% (1/58)	2% (1/58)

Hypopituitarism after TBI

- Positive correlation between peak GH levels and
  - Verbal learning
  - Verbal short-term memory (Popovic et al, 2004)
- Positive correlation between hypopituitarism and
  - Unfavorable body composition, sleep, energy, social isolation, overall quality of life (Klose et al, 2007)

Association Between Fatigue, Severity of Injury, Duration Since Injury, and Underlying Factors

Objective

- Examine the relationship between self-reported fatigue and the following potential factors:
  - Demographic characteristics
  - Injury characteristics
  - Sleep abnormalities
  - Affective symptomatology
  - Activity patterns and limitations
  - Substance use
  - Neuroendocrine findings

Research Questions

- Endocrine abnormalities not related to time since injury
- Endocrine abnormalities related to severity of injury
- Identify unique associations between types/levels of fatigue and underlying factors

Procedure

- Participants came to Santa Clara Valley Medical Center
- Session began between 8am and 10am
- All blood tests and questionnaires completed during the 4-hour protocol

Participants

- 119 individuals with TBI
  - at least 1 year post-injury
  - living in the community
  - 16 years of age or older
  - Able to give informed consent

Participants

- Exclude people with diseases/disorders known to produce fatigue
  - Cardiovascular/pulmonary disease, diabetes mellitus, rheumatoid arthritis, multiple sclerosis, cancer, known pituitary abnormalities, chronic fatigue syndrome, pregnancy

Measures

- Demographics
- Injury severity, duration, etiology
- Barroso Fatigue Scale
- Alcohol and substance use
- Pain VAS
- Pittsburgh Sleep Quality Index (PSQI)
- Beck Depression Inventory – II (BDI-II)
- Disability Rating Scale
- Craig Handicap Reporting and Assessment Technique (CHART)
  - Cognitive Independence, Occupation, Social Integration
- Neurobehavioral Functioning Inventory (NFI)
  - Somatic, Memory/attention difficulties, Motor impairment

Barroso Fatigue Scale

- 7 subscales: Intensity, ADLs, Socialization, General Impact, Mental Functioning, Timing, Relieving Factors, Aggravating Factors
- Contains
  - Fatigue Severity Scale (FSS)
  - Multidimensional Assessment of Fatigue (MAF) subscales: Severity, ADLs, Distress, Timing, Global Fatigue Index

Measures

- Baseline blood tests:
  - CBC
  - Fasting glucose
  - Fasting basal cortisol
  - Insulin growth factor-I
  - Thyroid (free T4, TSH)
  - Testosterone (males)
- Glucagon stimulation test to assess GH response (0.03 mg/kg im, 1 mg max)

Results

Demographics

- 78 males; 41 females
- Average age: 40±12 years (16-78)
- Duration of injury: 9±7.6 years (1-37)

Demographics

Marital Status	
Single	45% (53)
Married	27% (32)
Sep./Div./Wid.	29% (34)
Productive Activity	
Employed	50% (59)
Unemployed	37% (44)
Other	13% (16)

Injury Characteristics

Etiology	
MVA	63% (71)
Violence	11% (12)
Falls	13% (15)
Other	13% (14)
Duration of Unconsciousness	
<1 d	26% (30)
1 d - <1 wk	21% (24)
1 wk – < 2 wks	15% (14)
> 2 wks	38% (44)

Measurement Scores

- Disability Rating Scale: 2.4±2.0
- BDI-II: 16.0±10.9
- PSQI: 7.6±4.5
- CHART
  - Cognitive Independence: 76.4±20.1
  - Occupation: 62.5±31.3
  - Social Integration: 82.4±23.0
- NFI
  - Somatic: 51.0±10.2
  - Memory: 52.3±10.0
  - Motor: 49.2±10.2
- GFI: 26±12; FSS: 4.4±1.8

Neuroendocrine Results

Hypothyroid	12% (14)
Low cortisol (<15 mcg/dl)	64% (76)
Low testosterone (n=78)	15% (12)
Low IGF-1	19% (23)
Growth Hormone	
Severe deficiency (<3ng/ml)	34% (39)
Moderate deficiency (3-9.9 ng/ml)	31% (36)
Normal (≥ 10ng/ml)	35% (40)

Neuroendocrine Results

	IGF-1 Level	
	Low	Normal
Growth Hormone (n=59)		
Severe deficiency	6 (26%)	17 (74%)
Moderate deficiency	3 (19%)	13 (81%)
Normal	4 (20%)	16 (80%)

X^2=0.37; df(2); p=0.83

Time Since Injury and Endocrine Abnormalities

		Abnormal GH score	Abnormal Cortisol	Abnormal IGF-1	Abnormal T4 level	Abnormal Testosterone	Not Menstruating
Time since injury	*r*	.00	.00	.07	.00	.11	.00
	N	114	118	117	117	Men: 77	Women: 25

		Peak GH	Cortisol	IGF-1	T4 level	TSH	Testosterone
Time since injury	*r*	-.11	-.14	-.38**	-.09	.05	-.20*
	N	111	118	118	117	117	Men: 77

* $p < .05$ ** $p < .01$

Duration of Unconsciousness and Endocrine Abnormalities

		Abnormal GH score	Abnormal Cortisol	Abnormal IGF-1	Abnormal T4 level	Abnormal Testosterone	Not Menstruating
Duration of Unconscious	*r*	.00	.00	.14*	.00	.00	.00
	N	111	115	114	115	Men: 74	Women: 25

		Peak GH	Cortisol	IGF-1	T4 level	TSH	Testosterone
Duration of Unconscious	*r*	-.09	.09	.01	-.04	.01	-.02
	N	108	115	115	114	114	Men: 74

* $p < .05$ ** $p < .01$

Types/Levels of Fatigue and Associated Factors - Barroso

	Intensity Beta	ADLs Beta	Social Beta	Mental Beta	General Beta
Female	.28**	.26**	.17**	.25**	.17*
BDI-II	.30**	.30**	.44**	.25**	.41**
NFI Memory	.34**	---	---	.37**	---
NFI Motor	---	.30**	.24**	---	---
NFI Somatic	---	---	---	---	.21*
PSQI	.16*	---	---	---	---
CHART Social	---	.18*	---	---	---
Anti-depressant	---	---	.15*	---	---
F	33.78**	24.23**	26.47**	25.29**	22.18**
Adjusted R^2	.57	.54	.49	.40	.45

* $p < .05$ ** $p < .01$

Types/Levels of Fatigue and Associated Factors – MAF & FSS

	Severity Beta	ADLs Beta	Distress Beta	Timing Beta	GFI Beta	FSS Beta
Female	.18*	.30**	---	.25**	.21*	---
BDI-II	---	.25**	.46**	.27**	.28**	.35**
NFI Memory	.40**	---	---	.36**	.30**	---
Pain VAS	.39**	---	.22**	---	.30**	---
NFI Motor	---	.20*	---	---	---	.33**
CHART Social	---	-.21**	---	---	---	---
PSQI	---	.20*	---	---	---	---
Anti-depressant	---	---		---	---	-.19*
F	38.24**	17.55**	22.01**	26.51**	41.31**	25.28**
Adjusted R^2	.49	.46	.49	.42	.60	.43

* $p < .05$ ** $p < .01$

Different Types of Fatigue?

- Intensity (Barroso) – memory and sleep
- Severity (MAF) – memory and pain
- ADLs (Barroso) – motor and social
- ADLs (MAF) – motor, social and sleep
- Mental (Barroso) – memory
- General Impact (Barroso) - somatic

Limitations

- Selection bias of sample
- Cross-sectional nature
- Self-report

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