TAND: DEVELOPMENT, EMOTION AND BEHAVIOR IN TSC

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OVERVIEW

- TAND DEFINED
- TAND SPECTRUM
- TAND CLUSTERS
- TAND CLINICAL PHENOTYPES
- TAND TREATMENTS
- TAND TALES
- TAND TAKEAWAYS

TAND DEFINED

- "terminology to describe the interrelated functional and clinical manifestations of brain dysfunction in TSC, including aggressive behaviors, autism spectrum disorders, intellectual disabilities, psychiatric disorders, neuropsychological deficits, as well as school and occupational difficulties"

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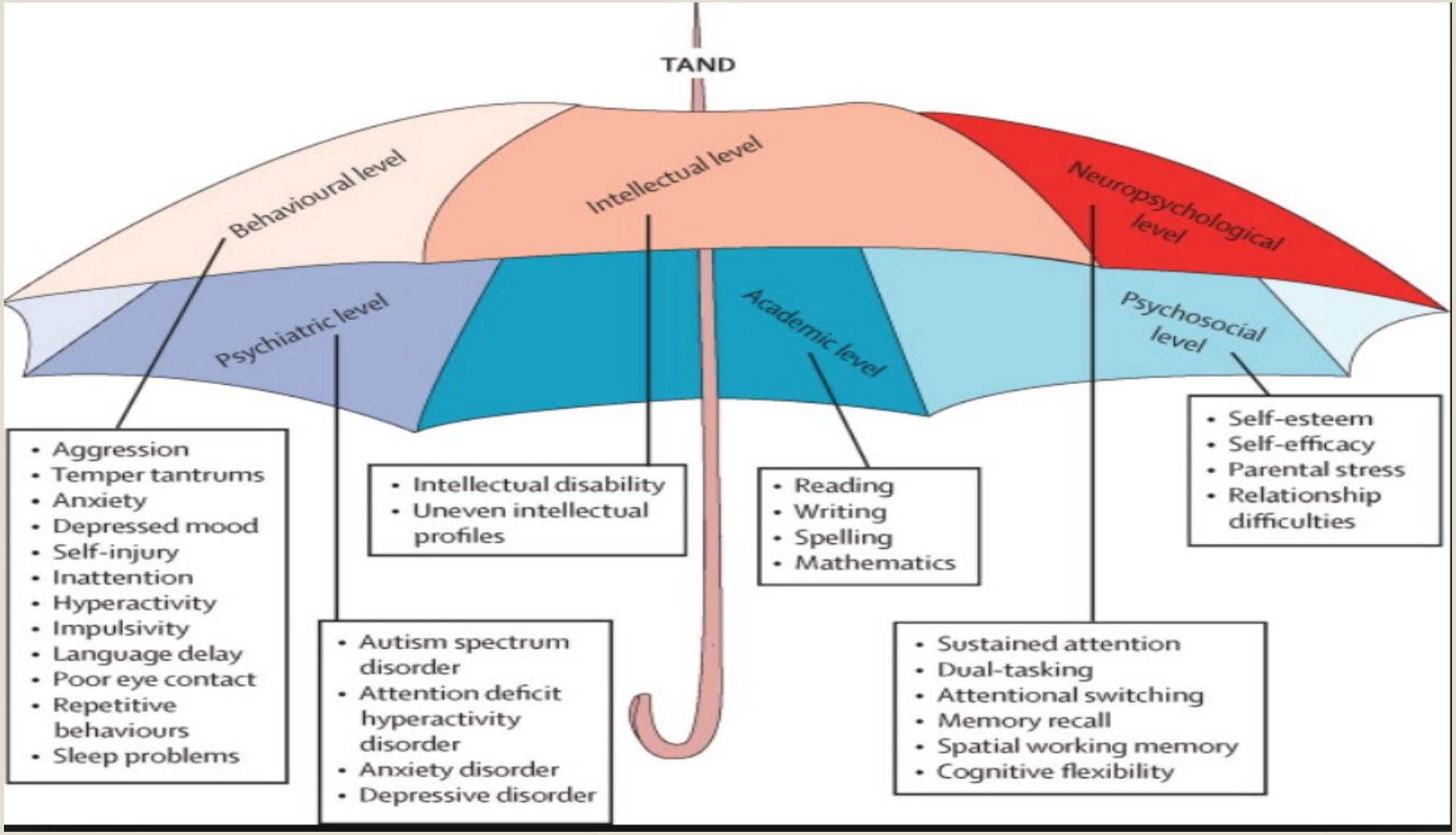
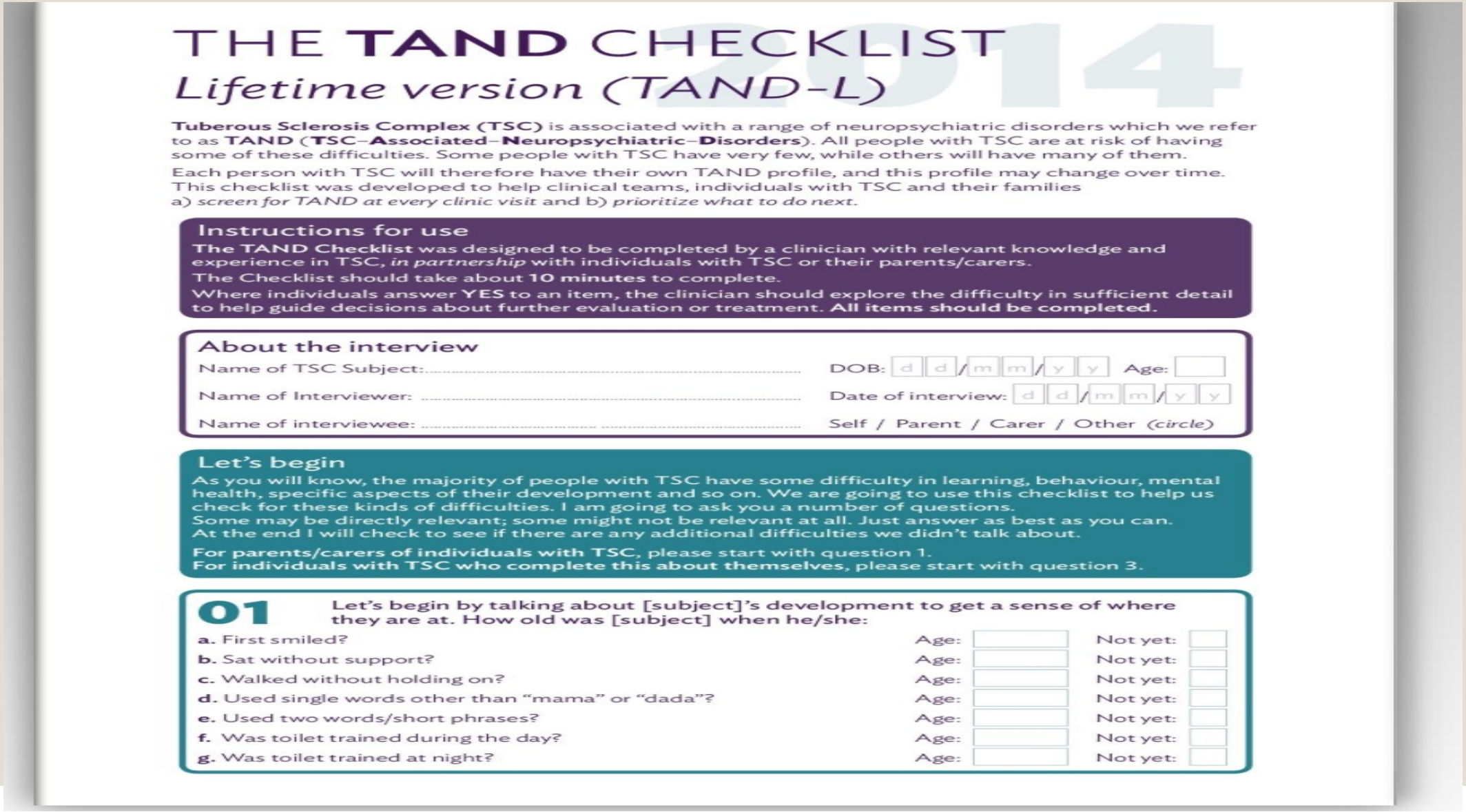
DeVries, et al.

TAND SPECTRUM



TAND CHECKLIST



THE **TAND** CHECKLIST

2014

Lifetime version (TAND-L)

Tuberous Sclerosis Complex (TSC) is associated with a range of neuropsychiatric disorders which we refer to as **TAND** (**TSC–Associated–Neuropsychiatric–Disorders**). All people with TSC are at risk of having some of these difficulties. Some people with TSC have very few, while others will have many of them.

Each person with TSC will therefore have their own TAND profile, and this profile may change over time. This checklist was developed to help clinical teams, individuals with TSC and their families a) *screen for TAND at every clinic visit* and b) *prioritize what to do next*.

Instructions for use

The TAND Checklist was designed to be completed by a clinician with relevant knowledge and experience in TSC, *in partnership* with individuals with TSC or their parents/carers.

The Checklist should take about **10 minutes** to complete.

Where individuals answer **YES** to an item, the clinician should explore the difficulty in sufficient detail to help guide decisions about further evaluation or treatment. **All items should be completed.**

About the interview

Name of TSC Subject: ..... DOB: d d / m m / y y Age: ____

Name of Interviewer: ..... Date of interview: d d / m m / y y

Name of interviewee: ..... Self / Parent / Carer / Other *(circle)*

Let's begin

As you will know, the majority of people with TSC have some difficulty in learning, behaviour, mental health, specific aspects of their development and so on. We are going to use this checklist to help us check for these kinds of difficulties. I am going to ask you a number of questions.
Some may be directly relevant; some might not be relevant at all. Just answer as best as you can.
At the end I will check to see if there are any additional difficulties we didn't talk about.

For parents/carers of individuals with TSC, please start with question 1.
For individuals with TSC who complete this about themselves, please start with question 3.

01 Let's begin by talking about [subject]'s development to get a sense of where they are at. How old was [subject] when he/she:

a. First smiled?	Age:		Not yet:	
b. Sat without support?	Age:		Not yet:	
c. Walked without holding on?	Age:		Not yet:	
d. Used single words other than "mama" or "dada"?	Age:		Not yet:	
e. Used two words/short phrases?	Age:		Not yet:	
f. Was toilet trained during the day?	Age:		Not yet:	
g. Was toilet trained at night?	Age:		Not yet:	

02 What is [subject]'s current level of *(please tick)*:

a. Language: ☐ non-verbal ☐ simple language ☐ fluent

b. Self-care: ☐ dependent on others ☐ some self-care skills ☐ independent

c. Mobility: ☐ wheelchair ☐ needs significant support ☐ some difficulty ☐ completely mobile

03 Let's talk about behaviours causing concern to you or to other people. Have/has [subject] ever had difficulty with any of the following?

a. Anxiety	NO ☐	YES ☐
b. Depressed mood	NO ☐	YES ☐
c. Extreme shyness	NO ☐	YES ☐
d. Mood swings	NO ☐	YES ☐
e. Aggressive outbursts	NO ☐	YES ☐
f. Temper Tantrums	NO ☐	YES ☐
g. Self-injury, such as hitting self, biting self, scratching self	NO ☐	YES ☐
h. Absent or delayed onset of language to communicate	NO ☐	YES ☐
i. Repeating words or phrases over and over again	NO ☐	YES ☐
j. Poor eye contact	NO ☐	YES ☐
k. Difficulties getting on with other people of similar age	NO ☐	YES ☐
l. Repetitive behaviours, *such as doing the same thing over and over again*	NO ☐	YES ☐
m. Very rigid or inflexible about how to do things or not liking change in routines	NO ☐	YES ☐
n. Overactivity/hyperactivity, *such as being constantly on the go*	NO ☐	YES ☐
o. Difficulty paying attention or concentrating	NO ☐	YES ☐
p. Restlessness or fidgetiness, *such as wriggling or squirming*	NO ☐	YES ☐
q. Impulsivity, *such as butting in, not waiting turn*	NO ☐	YES ☐
r. Difficulties with eating, *such as eating too much, too little, unusual things*	NO ☐	YES ☐
s. Sleep difficulties, *such as with falling asleep or waking*	NO ☐	YES ☐
If you answered YES to any of the above:		
Have you had further evaluation or support for it?	NO ☐	YES ☐
Would you like to have further evaluation or support for it?	NO ☐	YES ☐

04 Problem behaviours may add up to meet criteria for specific psychiatric disorders. Have/has [subject] ever received a diagnosis of:

a. Autism Spectrum Disorder (ASD), *including autism, Asperger's*	NO ☐	YES ☐
b. Attention Deficit Hyperactivity Disorder (ADHD)	NO ☐	YES ☐
c. Anxiety Disorder, *including as panic, phobia, separation anxiety disorder*	NO ☐	YES ☐
d. Depressive Disorder	NO ☐	YES ☐
e. Obsessive Compulsive Disorder	NO ☐	YES ☐
f. Psychotic Disorder, *including schizophrenia*	NO ☐	YES ☐
If you answered YES to any of the above		
Have you had further evaluation or support for it?	NO ☐	YES ☐
Would you like to have further evaluation or support for it?	NO ☐	YES ☐

05 About half of people with TSC will have significant difficulties in their overall intellectual development and may have 'intellectual disability'.

a. Have you ever been concerned about this for [subject]? NO ☐ YES ☐

b. Have/has [subject] ever had a formal evaluation of intelligence by a professional using IQ-type tests? NO ☐ YES ☐

If YES, what did results show?

- Normal Intellectual Ability (IQ > 80) ☐
- Borderline Intellectual Ability (IQ 70-80) ☐
- Mild Intellectual Disability (IQ 50-69) ☐
- Moderate Intellectual Disability (IQ 35-49) ☐
- Severe Intellectual Disability (IQ 21-34) ☐
- Profound Intellectual Disability (IQ <20) ☐

c. What is your view of [subject]'s intellectual ability?

- Normal Intellectual Ability ☐
- Mild-Moderate Intellectual Disability ☐
- Severe - Profound Intellectual Disability ☐

d. Would you like to have further evaluation or support for it? NO ☐ YES ☐

06 Many people with TSC who are of school age will have difficulty in school.

[For individuals of school age]: Does/do [subject] have any difficulty with any of the following:
[For individuals after school age]: Did [subject] have any difficulty with any of the following:

a. Reading	N/A ☐	NO ☐	YES ☐
b. Writing	N/A ☐	NO ☐	YES ☐
c. Spelling	N/A ☐	NO ☐	YES ☐
d. Mathematics	N/A ☐	NO ☐	YES ☐
If you answered YES to any of the above			
Have/has [subject] had further evaluation or support for it?		NO ☐	YES ☐
Have/has [subject] been considered for any additional support in school such as extra help or an Individual Educational Plan (IEP)?		NO ☐	YES ☐
Would you like to have further evaluation or support for [subject]?		NO ☐	YES ☐

07 The majority of people with TSC will have some difficulties in some specific brain skills. Do/does [subject] have difficulty with any of the following:

a. Memory, *such as remembering things that have happened*	NO ☐	YES ☐
b. Attention, *such as concentrating well, not getting distracted*	NO ☐	YES ☐
c. Dual-tasking/ Multi-tasking, *such as doing 2 tasks at the same time*	NO ☐	YES ☐
d. Visuo-spatial tasks, *such as solving puzzles or using building blocks*	NO ☐	YES ☐
e. Executive skills, *such as planning, organizing, flexible thinking*	NO ☐	YES ☐
f. Getting disoriented, *such as not knowing the date or where you are*	NO ☐	YES ☐
If you answered YES to any of the above		
Have/has [subject] had further evaluation or support for it?	NO ☐	YES ☐
Would you like to have further evaluation or support for these difficulties?	NO ☐	YES ☐

08 Apart from the challenges listed above, TSC can have a big impact on people's lives in other ways. Have/has [subject] had any difficulties with:

a. Low self-esteem — NO ☐ YES ☐
b. Very high levels of stress in families, for instance between *siblings* — NO ☐ YES ☐
c. Very high levels of stress between *parents* leading to significant relationship difficulties — NO ☐ YES ☐

If you answered YES to any of the above
Have/has [subject] and/or your family had further evaluation or support for it? — NO ☐ YES ☐
Would you like to have further evaluation or support for it? — NO ☐ YES ☐

09 Taking together all the difficulties discussed above, how much have these bothered, troubled or distressed you/your child/family?

Not at all 0 1 2 3 4 5 6 7 8 9 10 Extremely

10 Of all the concerns listed above, what are your top priorities to work on next?

a. .....
b. .....
c. .....

11 Do you have any other worries about TAND for [subject] that we have not talked about as we went through the checklist?

NO ☐ YES ☐ If YES, please list: .....

Thank You!

12 Interviewer's judgement of impact/burden on the individual/child/family.

Not at all 0 1 2 3 4 5 6 7 8 9 10 Extremely

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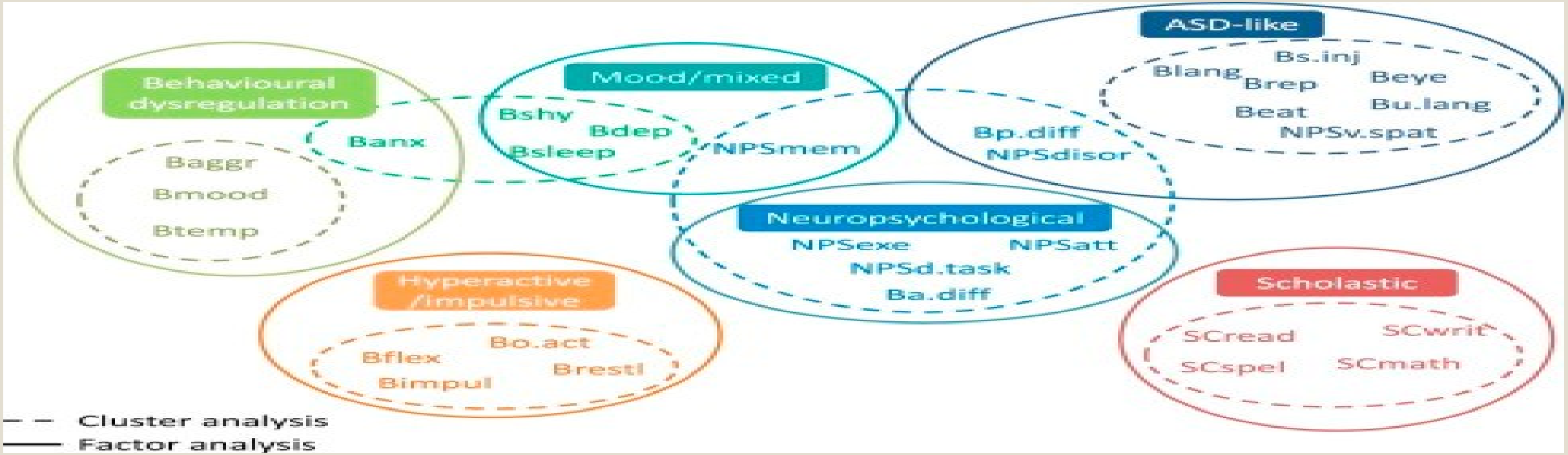
TAND CLUSTERS



Is It Feasible to Identify Natural Clusters of TSC-Associated Neuropsychiatric Disorders (TAND)?

Leclezio L, Gardner-Lubbe S, de Vries PJ.

Pediatr Neurol. 2018 Apr;81:38-44. doi: 10.1016/j.pediatrneurol.2017.12.006. Epub 2018 Jan 31.

PMID: 29530301

TAND UNIT







TAND CLINICAL PHENOTYPES





TAND CLINICAL PHENOTYPES

External

- ADHD
- ODD
- Conduct Disorder
- Aggression
- Self-injury
- Autism
- OCD

Internal

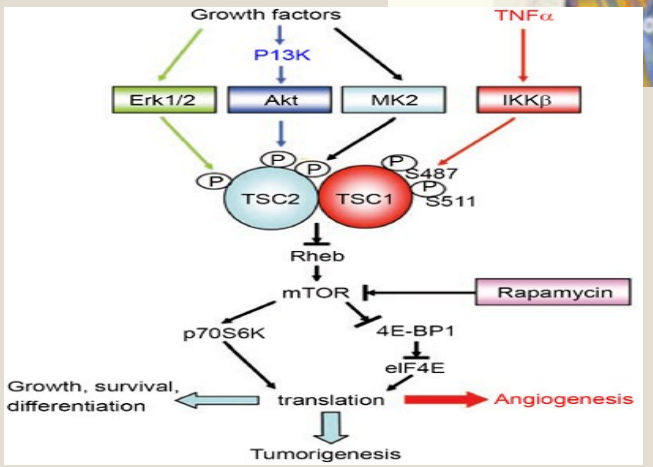
- Anxiety
- Pragmatic language impairment
- Depression
- Adjustment disorder

TAND TREATMENTS

- Functional
- Symptomatic
- Organic







MEREDITH

- Meredith is an 18 year old young lady with clinically definite, genetically confirmed Tuberous Sclerosis. Her mother reports that her seizures have resolved, she has no cognitive concerns; however, she became so worried that she could no longer attend school. She has been homeschooled for the last 2 years, has no friends and is tearful upon examination.

MEREDITH

- **TAND Evaluation:**
  - Cognitive-sparing TSC with anxiety and pragmatic language impairment
- FUNCTIONAL
  - No outward-facing behaviors
- Symptomatic
  - Anxiety
- Organic - None

MEREDITH

- **FUNCTIONAL**
- Individual CBT and social group for anxiety and social withdrawal.
- Respite - involvement in dance/music, sibling support, maternal counseling (father refused)

- **SYMPTOMATIC**
- SSRI for anxiety

- **ORGANIC**
- None indicated

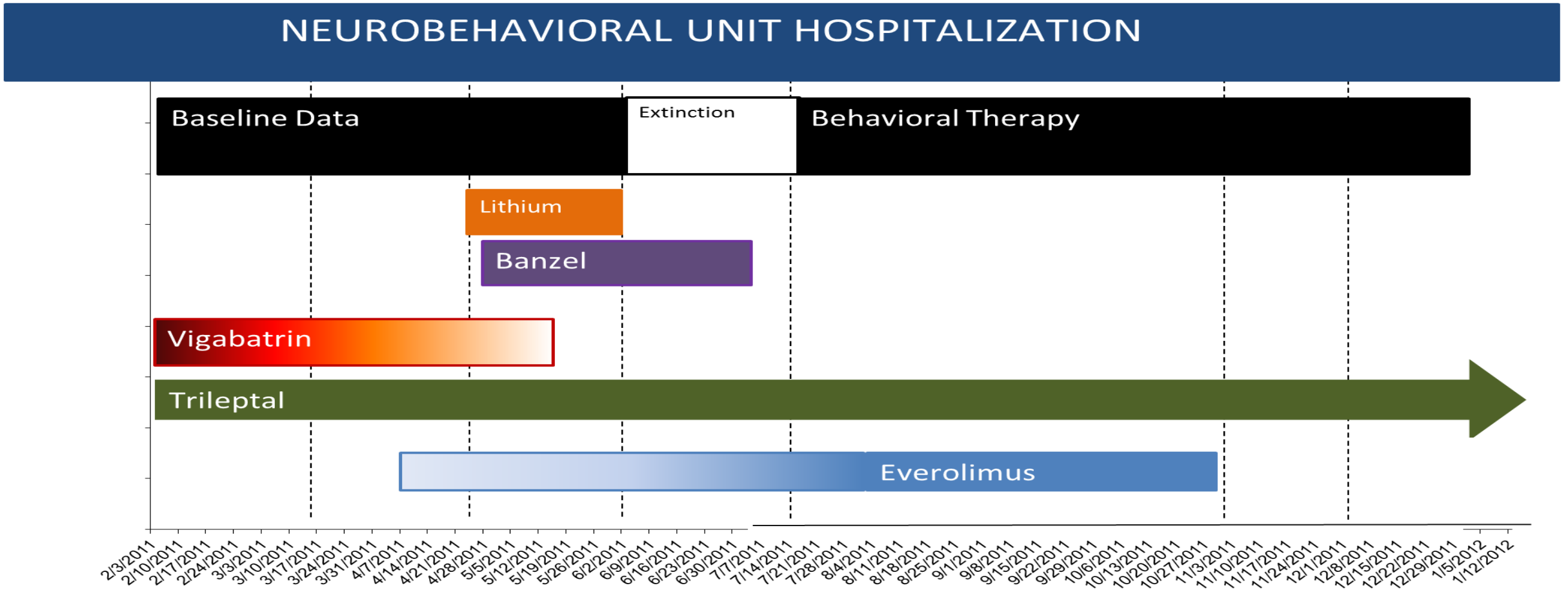
MEREDITH

- Maternal relief
- Completed her first year in community college with a circle of friends (rote learning to avoid dangerous social situations)
- Attending concerts with friends, dancing/singing performances and considering volunteering with the elderly

JACK

- Jack is a 17 year old young man with TSC-associated autism. His parents report that over the years he has become increasingly aggressive and self-injurious. When he began to violently attack his younger brother and his mother, they made the decision to place Jack in a residential school. His mother becomes tearful upon remembering the initial decision. In this facility, he has harmed more staff than anyone in his state.

JACK


NEUROBEHAVIORAL UNIT HOSPITALIZATION
Baseline Data
Extinction
Behavioral Therapy
Lithium
Banzel
Vigabatrin
Trileptal
Everolimus
2/3/2011
2/10/2011
2/17/2011
2/24/2011
3/3/2011
3/10/2011
3/17/2011
3/24/2011
3/31/2011
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4/14/2011
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8/11/2011
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9/15/2011
9/22/2011
9/29/2011
10/6/2011
10/13/2011
10/20/2011
10/27/2011
11/3/2011
11/10/2011
11/17/2011
11/24/2011
12/1/2011
12/8/2011
12/15/2011
12/22/2011
12/29/2011
1/5/2012
1/12/2012

JACK

- Functional
  - What in the environment might be maintaining the behaviors?
    - Aggression
      - Escape
        - Transitions
        - Academic tasks
        - Daily living tasks
      - Access to attention
    - Self-injury – none

JACK

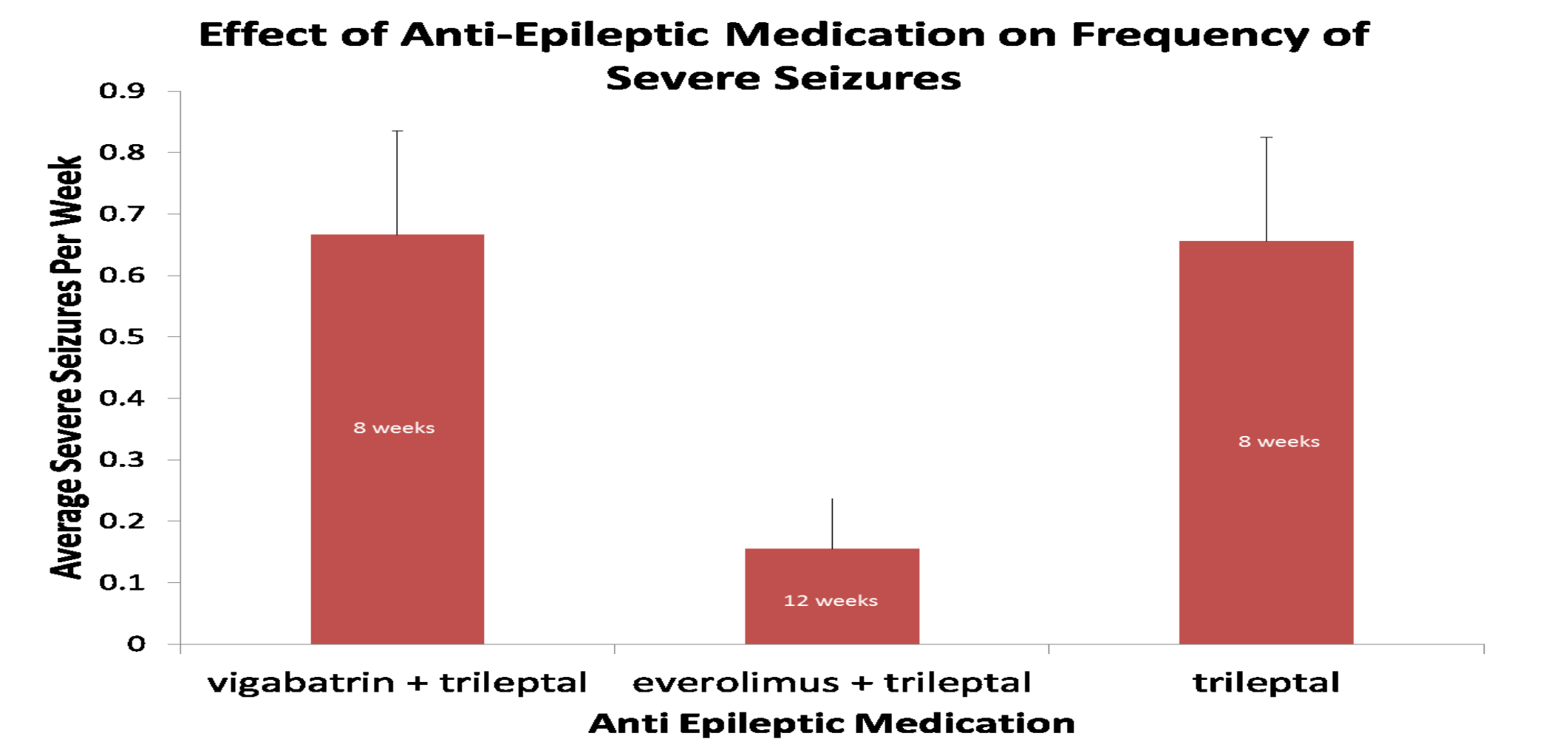
- Symptomatic
  - Epilepsy
    - Oxcarbazepine
    - Vigabatrin
  - Aggression
    - Lithium
    - Asenapine

JACK

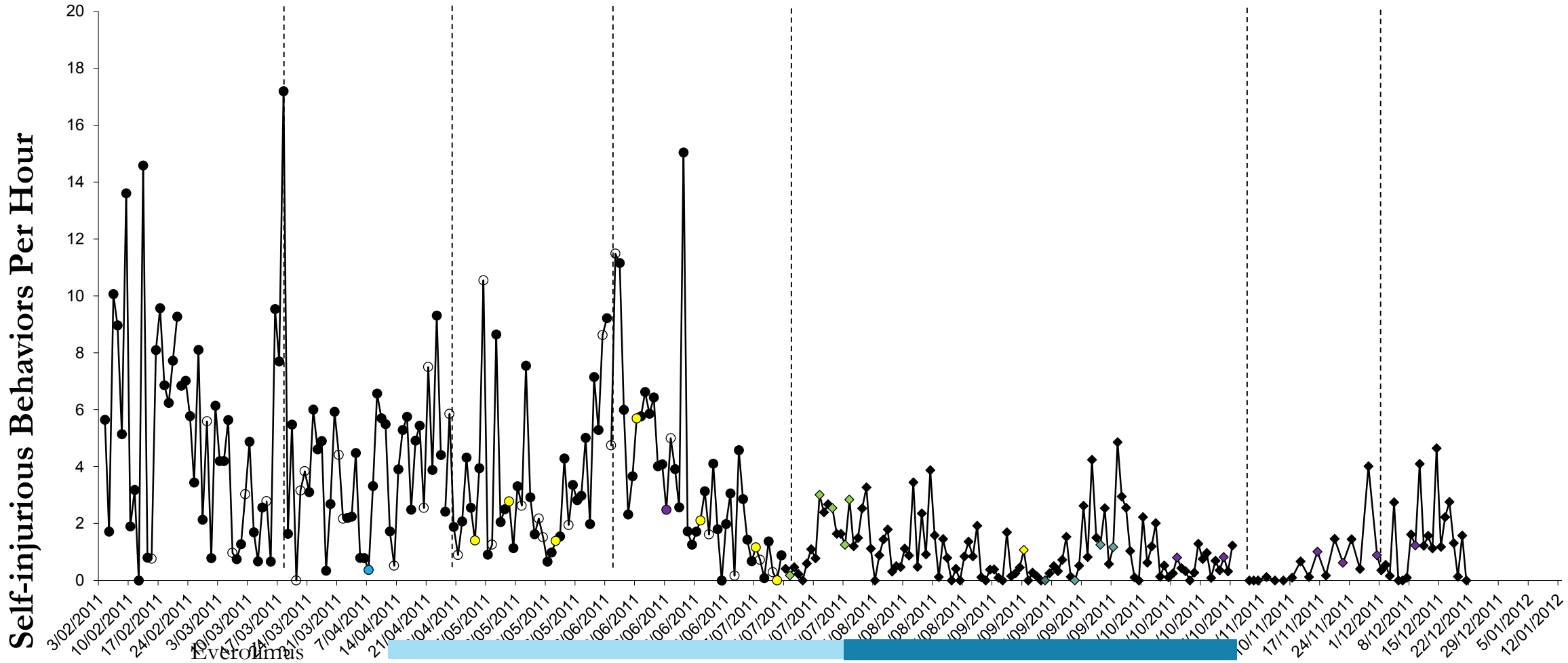
- Organic
  - Subependymal giant cell astrocytoma
    - Everolimus (mTOR inhibitor)

  - Aggression
    - Lithium (inositol-1 phosphate inhibitor)
      - ? mTORC2 inhibition

JACK


Effect of Anti-Epileptic Medication on Frequency of Severe Seizures
Average Severe Seizures Per Week
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
8 weeks
12 weeks
8 weeks
vigabatrin + trileptal
everolimus + trileptal
trileptal
Anti Epileptic Medication

JACK


Self-injurious Behaviors Per Hour
20
18
16
14
12
10
8
6
4
2
0
3/02/2011
10/02/2011
17/02/2011
24/02/2011
3/03/2011
10/03/2011
17/03/2011
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Everolimus
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29/12/2011
5/01/2012
12/01/2012

JACK



JACK

Epilepsy & Behavior Case Reports 1 (2013) 122–125

Contents lists available at ScienceDirect

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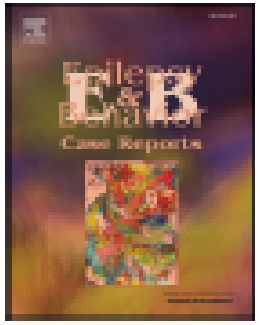
journal homepage: www.elsevier.com/locate/ebcr



Case Report

Everolimus and intensive behavioral therapy in an adolescent with tuberous sclerosis complex and severe behavior☆,☆☆,★

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TAND TAKEAWAYS

- **H**elp
- Parents, Extended Family, Professional
- *Inter*disciplinary, coordinated medical team
- TS Alliance, TSC international, Regional TS Alliance
- Social media

- **O**pportunities
- To aid others
- To identify new treatment strategies

- **P**ace
- Think marathon

- **E**xpectations
- Crystal clear
- Don't focus on the worst
- Things **can** and ***will*** get better

TAND TEAM COMMITMENT

- Global outreach platform to provide advocacy, education and guidance of care for individuals with TSC-associated neuropsychiatric disorders AND their families
- ***regardless of the ability to pay.***