

Epilepsy & depression: setting the scene

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8th AOEC - Epilepsy and Society

Programme

21-10-2010

Depression in people with epilepsy

1. What is depression?
2. How common is it in people with epilepsy?
3. Why does it matter?
4. What causes it?
5. What can be done about it?

WC Fields (1880-1926)



Start every day off with a
smile and get it over
with.

1. What is depression?

- It's not normal sadness
- It's not normal grief
- It's not normal, passing 'bad mood', 'grumpiness'
- It's not a type of personality
- It's not (wholly, solely) invented by
 - Psychiatrists, psychologists
 - Drug companies

It's a more

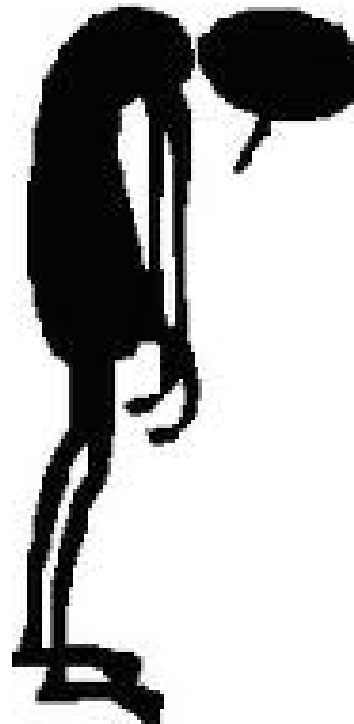
...sustained

...severe

...impairing

...state of mind

...and body



Thinking

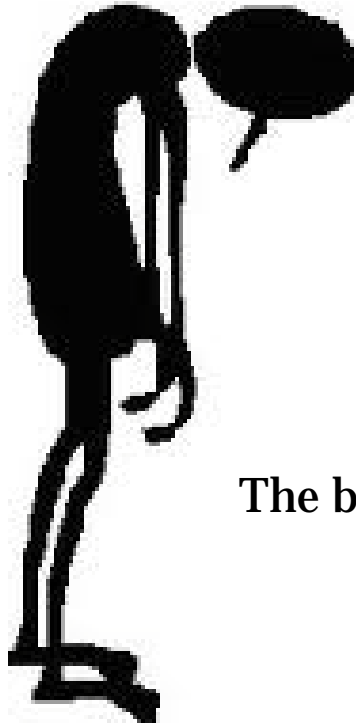
Cognition

Emotion

The body

It's a more
...sustained
...severe
...impairing

...state of mind
...and body



Thinking

Negative thoughts about
-the self
-the future
-the world

Rumination

Thought of death
or suicide

Cognition

Difficulty concentrating
Forgetfulness
Indecisiveness

Emotion

Sadness
Inability to feel
Anxiety, dread
Guilt
Inability to enjoy things
Loss of interest

The body

Loss of sexual interest
Sleep disturbance, insomnia
Fatigue, low energy
Loss of appetite (or gain)
Loss of weight
Slowed movement or agitated movement
Aches & pains
Menstruation may stop

Types of depression

Major depression

- Mild
- Moderate
- Severe
 - Severe with psychotic symptoms

- Depression as part of Bipolar Disorder
- Dysthymic disorder
- Postnatal depression
- Atypical depression
- ...

Is there a special type of depression that occurs just in epilepsy?

- **INTERICTAL DYSPHORIC DISORDER (IDD)**
 - Brief (hours/days)
 - Mixed and changing symptoms, 3 groups...
 - Fluctuating depressed mood, low energy, pain, insomnia
 - Fluctuating panic-like symptoms or anxiety
 - Irritability, unstable euphoria

2. How common is it?

Psychiatric Disorder	Controls	Patients With Epilepsy
Major depressive disorder	10.7%	17.4%
Anxiety disorder	11.2%	22.8%
Mood/anxiety disorder	19.6%	34.2%
Suicidal Ideation	13.3%	25.0%
Others	20.7%	35.5%

3. Why does it matter?

- **Suffering & misery**
- **Risk of suicide**
- **Impact on others**
 - Family, friends, children, carers
- **Impact on the ability to look after one's own health & wellbeing**
 - taking one's AEDs (adherence)
 - healthy eating, physical activity, social interaction
 - Impact on 'comorbid physical illness'
- **Impact on ability to function**

3. Why does it matter?

- Suffering & misery of the depressed person
- Risk of suicide
- Impact on others
 - Family, friends, children, carers
- Impact on the ability to look after one's own health
 - E.g., taking one's AEDs (adherence)
 - healthy eating, physical activity, social interaction
 - Impact on 'comorbid physical illness'
- Impact on ability to function
- **Impact on the epilepsy itself ?**
 - ***Topic of increasing research interest***

4. What causes depression?

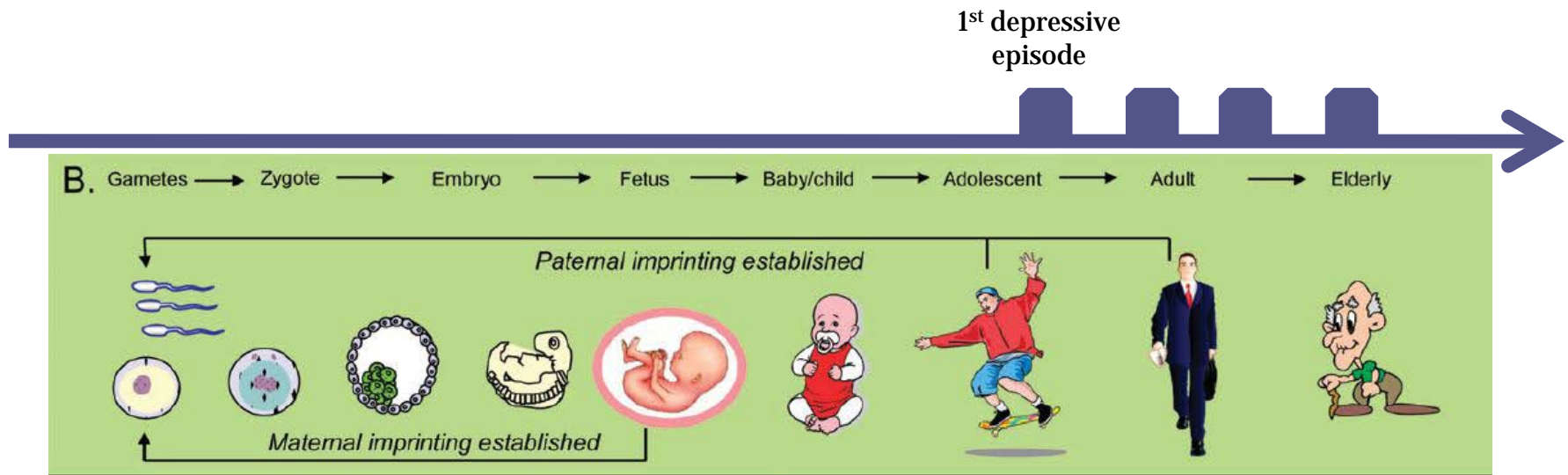
Two main points

1. It's due to an interaction of stress & vulnerability

- Not every who suffers stress/loss gets depressed. Why?
- Why does the same person cope well with one stress, then get depressed following another?
- What accounts for vulnerability? What accounts for resilience?
- Why does stress cause depression in one person, cause panic attacks in another, and alcohol abuse in a third?

2. A whole-of-life-course perspective

- Origins of depression vulnerability are in very early life
- One episode makes it easier to get more



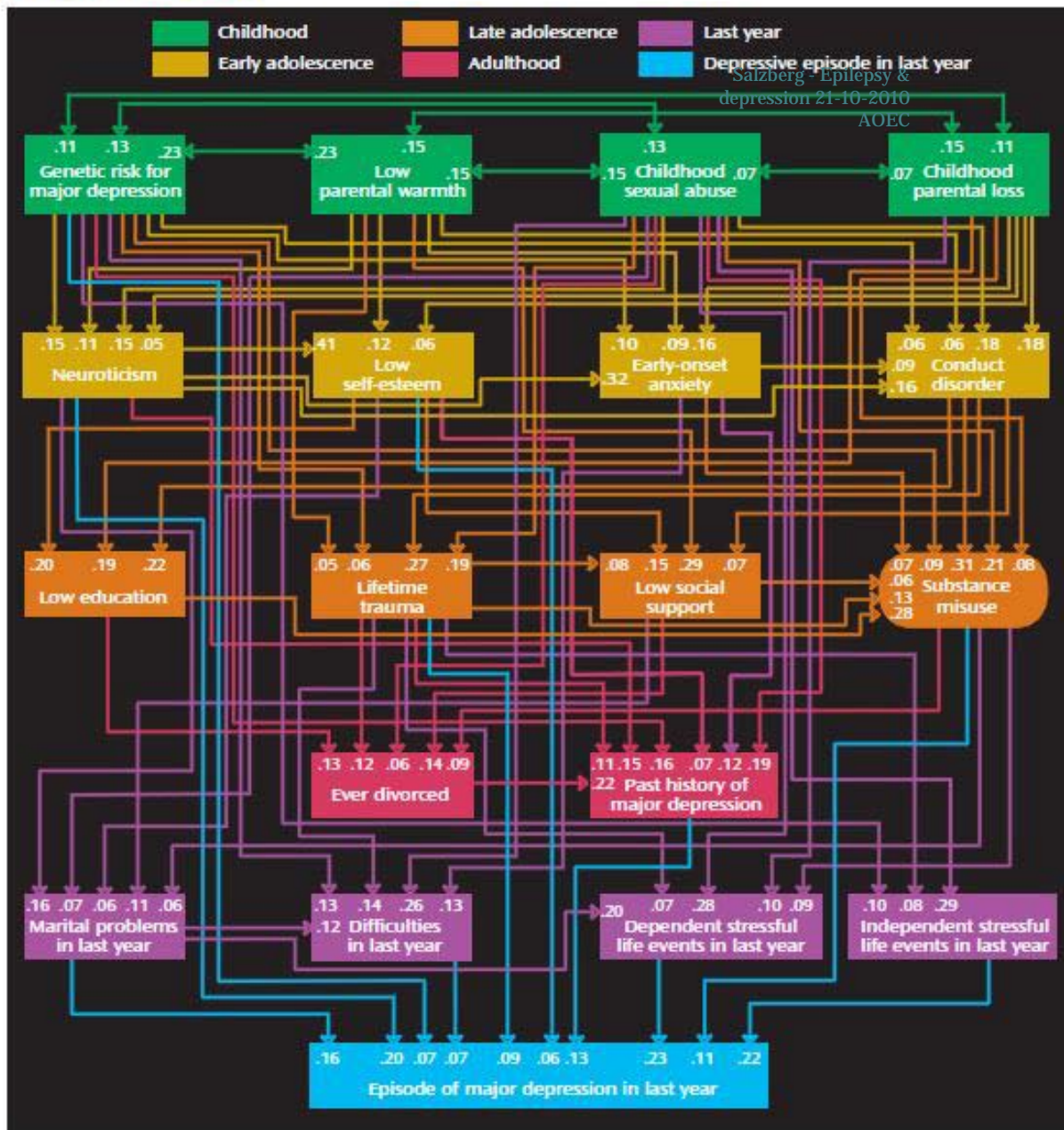
- Prenatal stress
- Genetic inheritance
- Epigenetic processes across generations
- 'Programming' of stress hormone responses

- Early life experience
 - good & bad experiences
 - acute or chronic stress or trauma
- Loss of significant others, e.g., bereavement
- Brain injury
 - infection, trauma etc
- Personality development
- Effects of stress on brain

- Stresses of
 - Work
 - Relationships
 - Money
 - Education
 - Etc
- Social support, social connection
- Psychological trauma

- 'Kindling' effects
 - One episode predisposes to another

- Brain changes & diseases of later life, eg, vascular disease

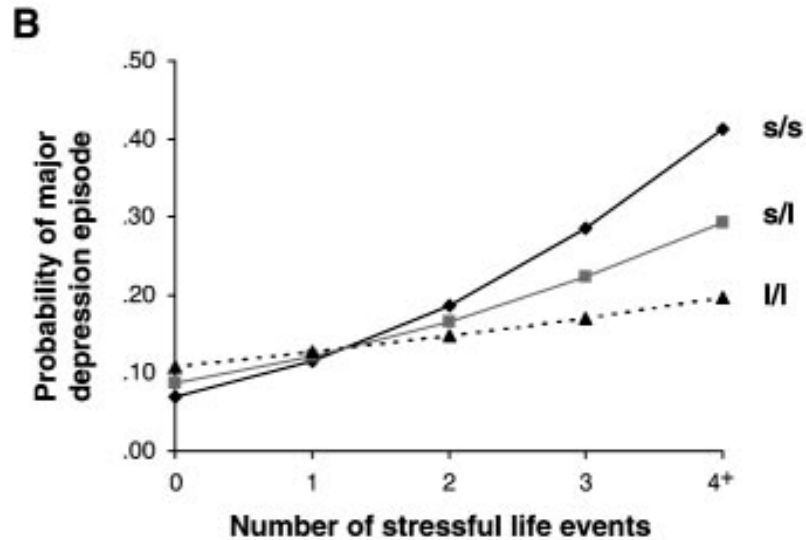


^a Two-headed arrows represent correlation coefficients. One-headed arrows represent path coefficients or standardized partial regression coefficients. Latent variables—indexed by observed variables in a measurement model—are depicted in ovals while observed variables are depicted in rectangles. All variables have estimated residual variance not depicted in the figure. See text for a description of the variables.

DEPRESSION

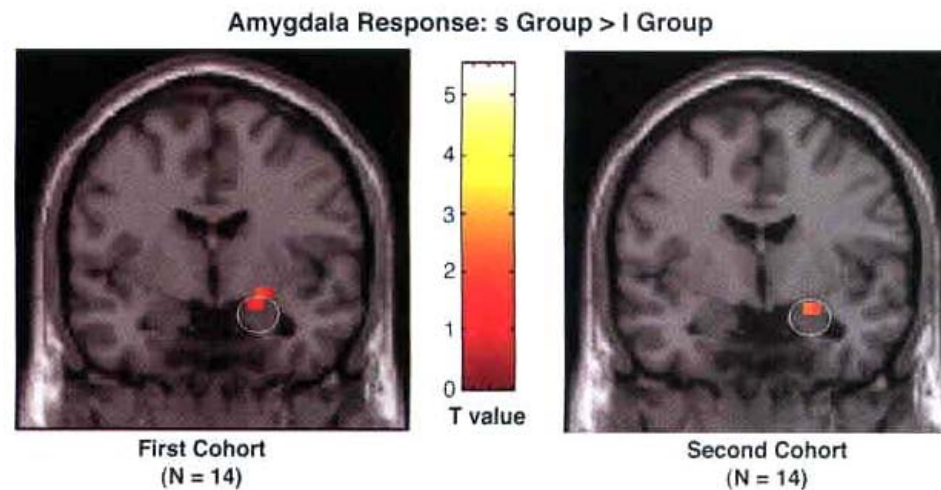
Caspi et al (2003) SCIENCE

- Dunedin birth cohort study, n~850 , followed 0-26 years, ~96% retention
- serotonin transporter polymorphism: s/s 17% s/l 51% l/l 31%



serotonin transporter

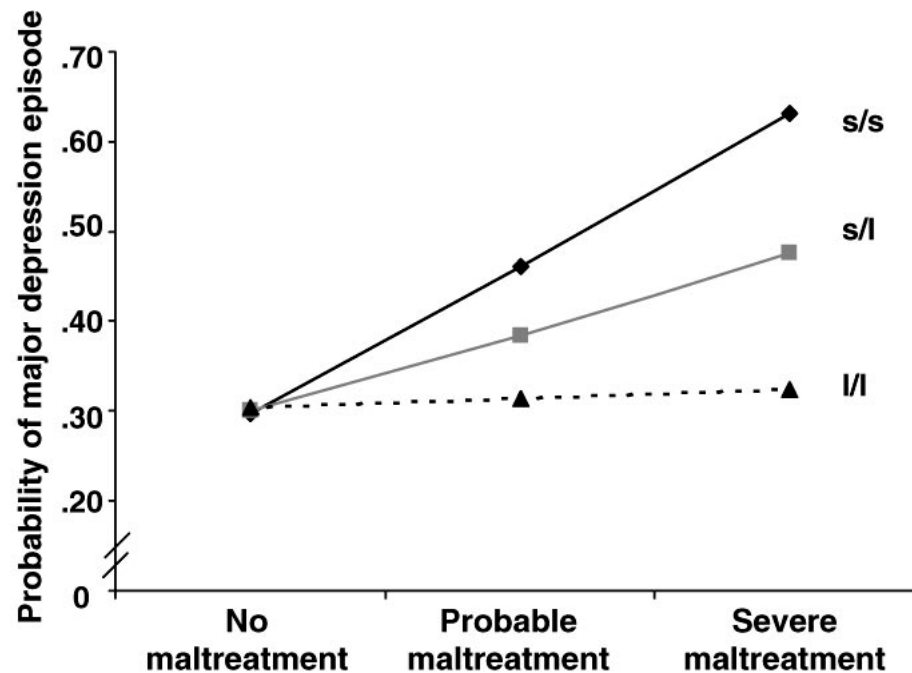
-genetic variants in population: s vs l



serotonin polymorphism and

- ...stress reactivity
- ...amygdala response to angry/fearful faces (Hariri et al SCIENCE 2002)

Early life stress



Caspi et al 2003 SCIENCE Dunedin Study

- association between early life maltreatment & depression at age 25

Causation of TLE: 3 stage model

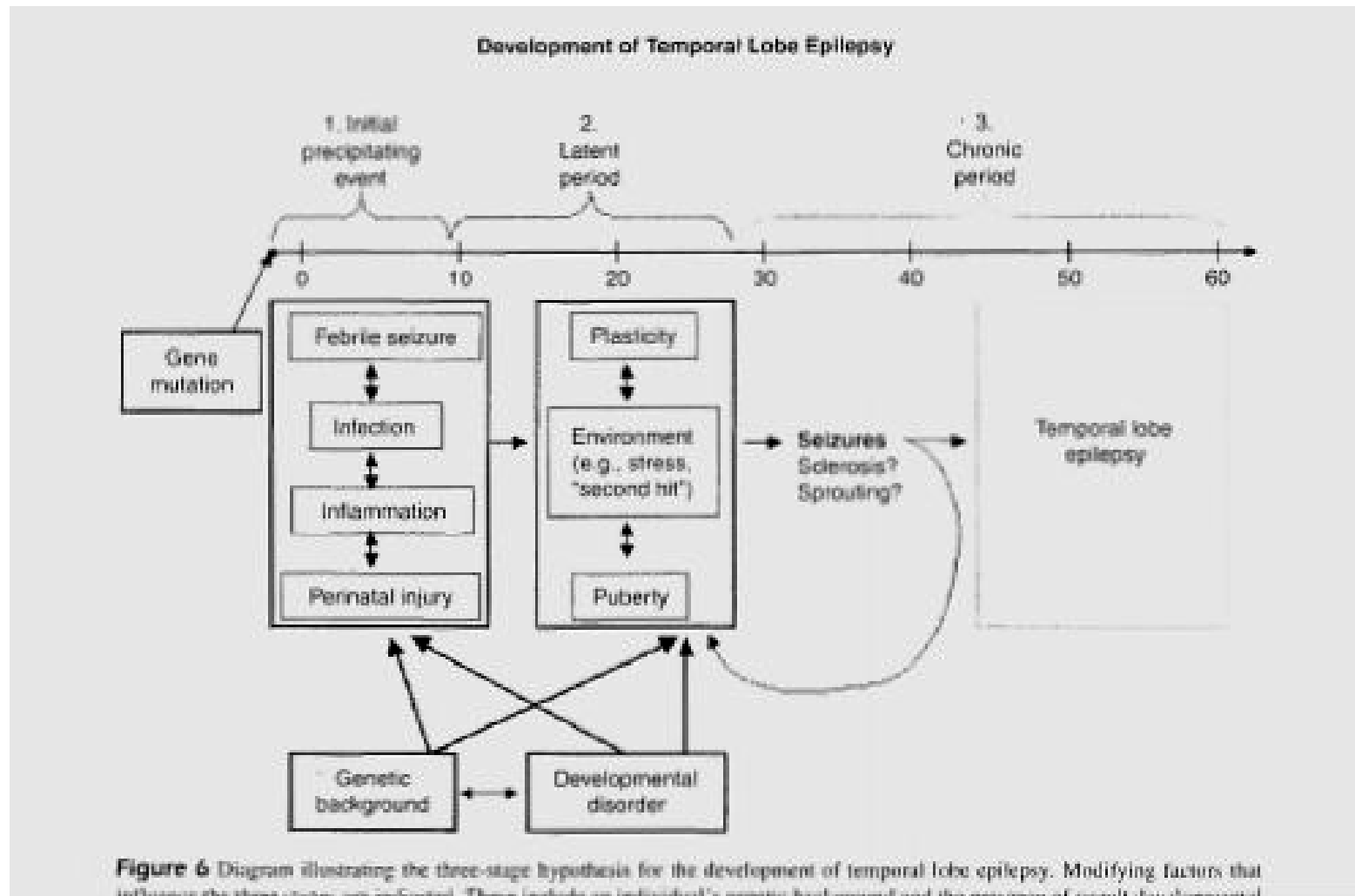


Figure 6 Diagram illustrating the three-stage hypothesis for the development of temporal lobe epilepsy. Modifying factors that influence the three stages are indicated. These include an individual's genetic background and the presence of occult developmental abnormalities.

Potential stress effects in TLE

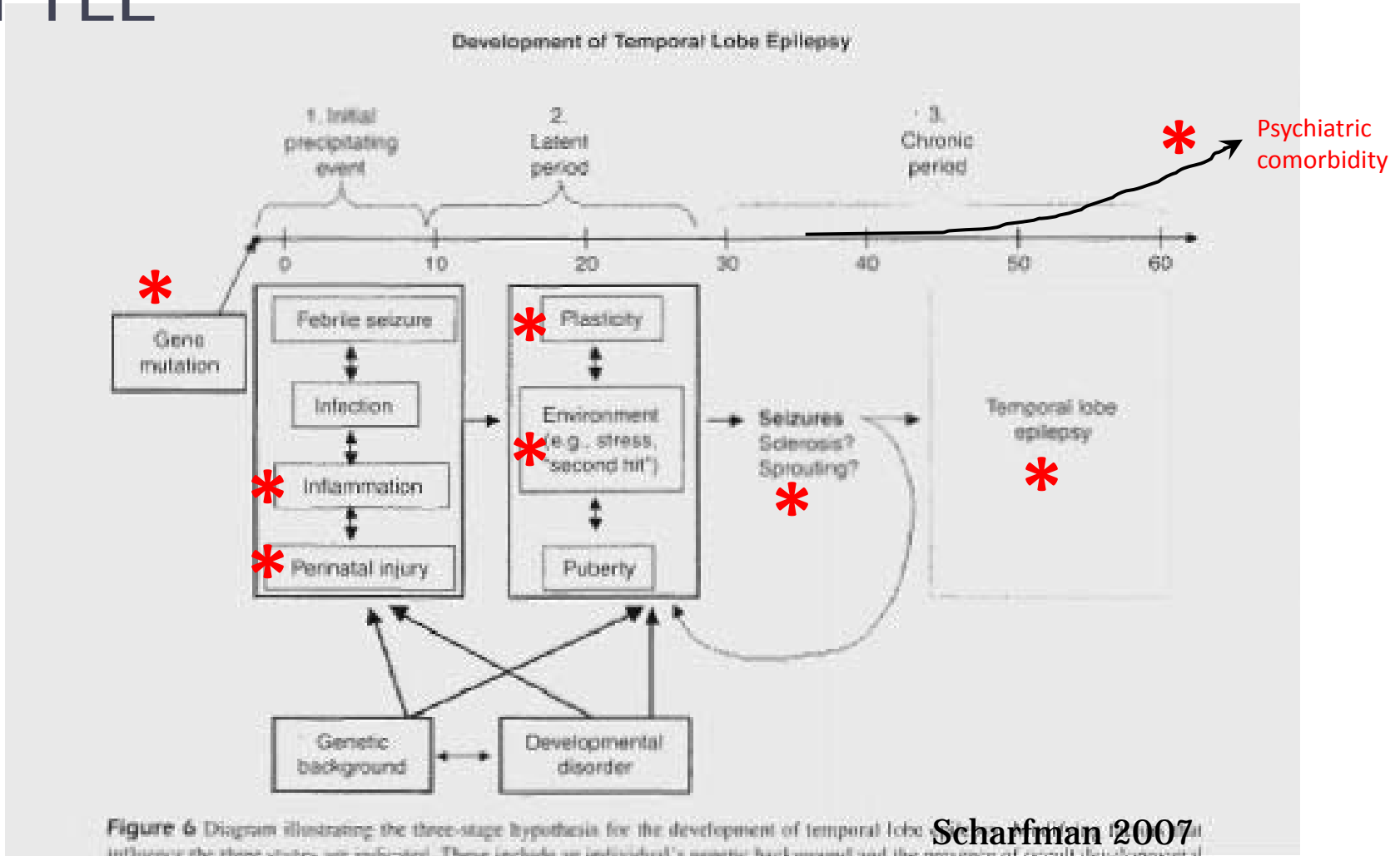


Figure 6 Diagram illustrating the three-stage hypothesis for the development of temporal lobe epilepsy. Red asterisks indicate factors that influence the three stages. These include an individual's genetic background and the presence of occult developmental abnormalities. **Scharfman 2007**

Potential stress effects in TLE

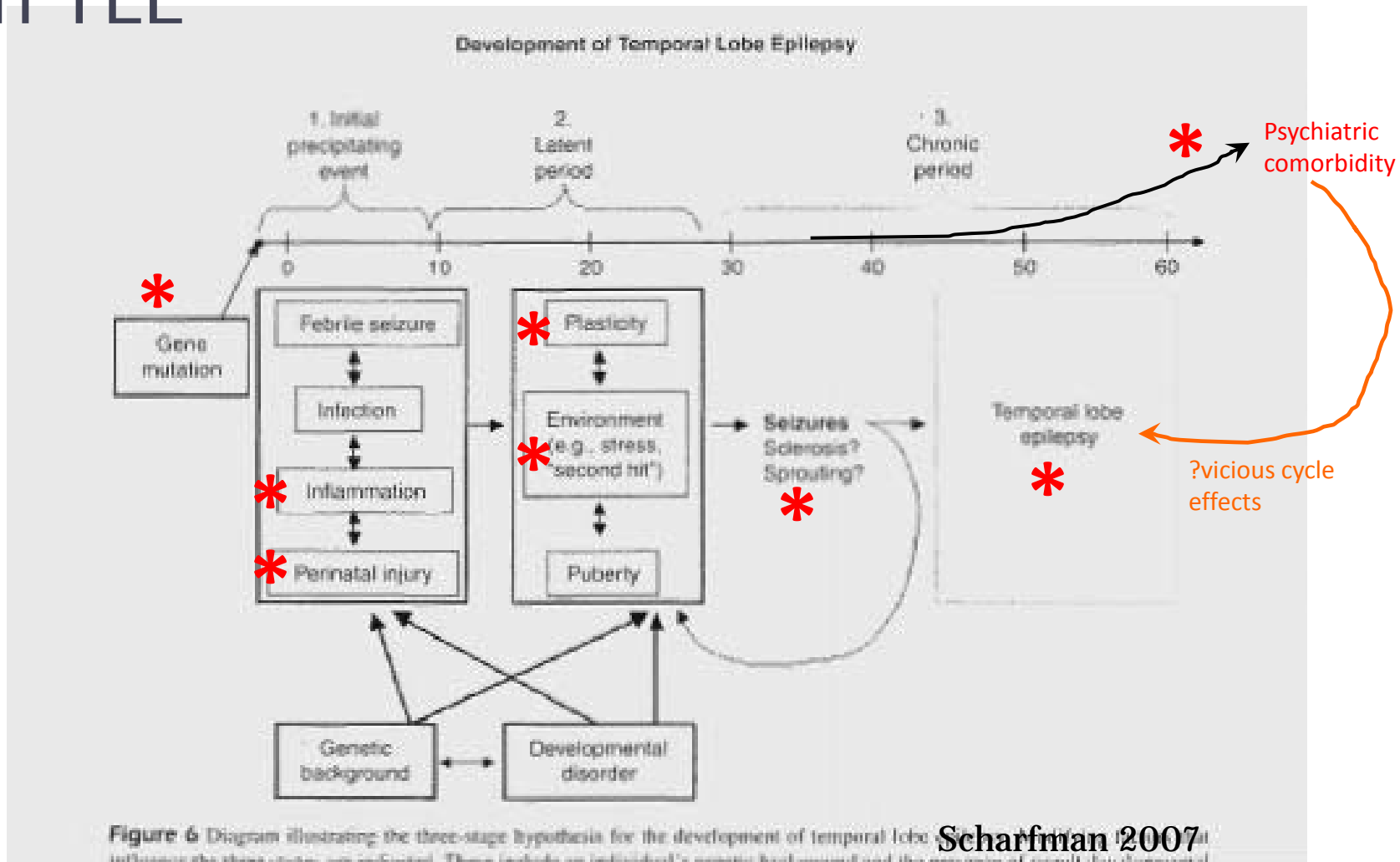
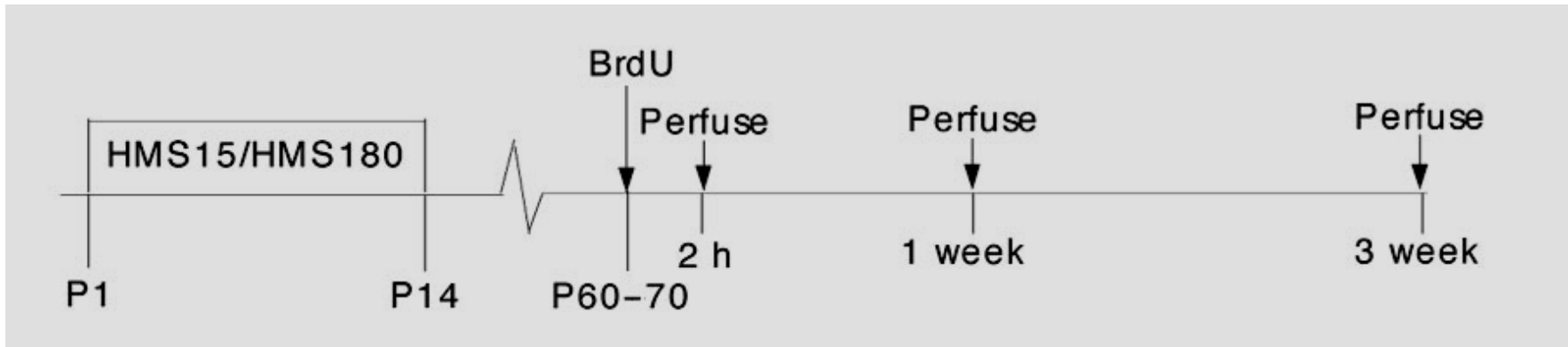


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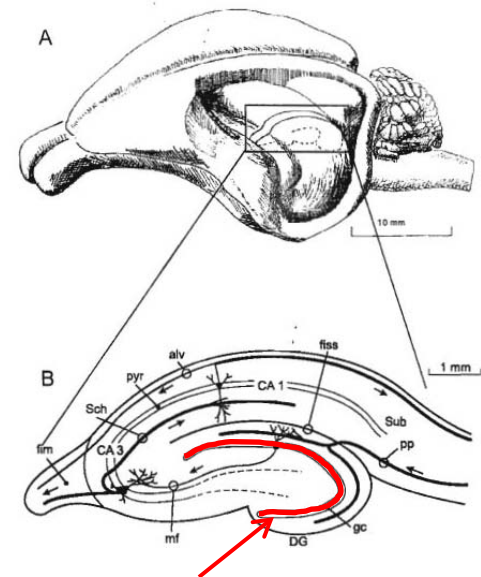
Example:

early life stress → neurogenesis in adulthood

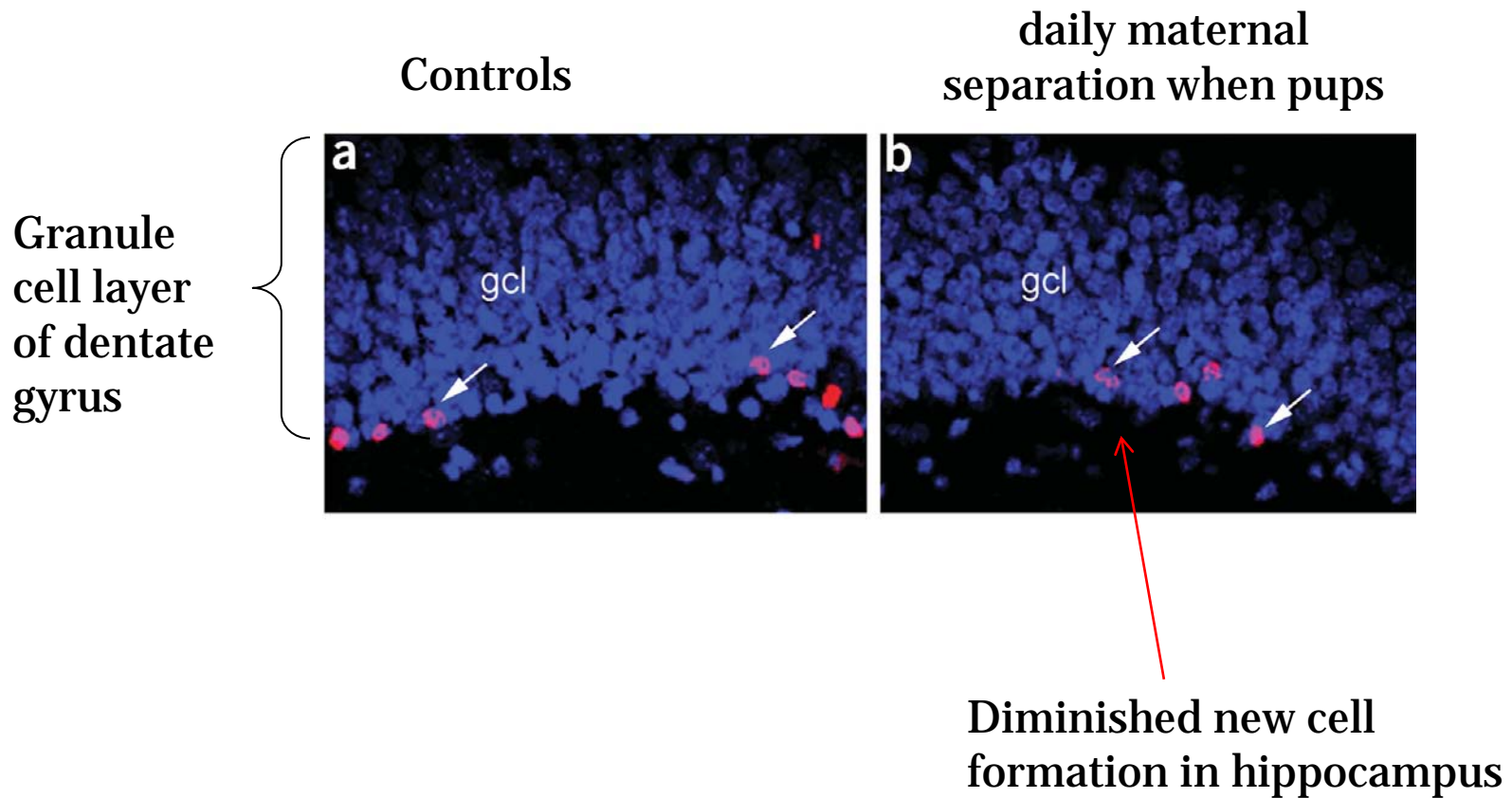


3 GROUPS OF RATS:

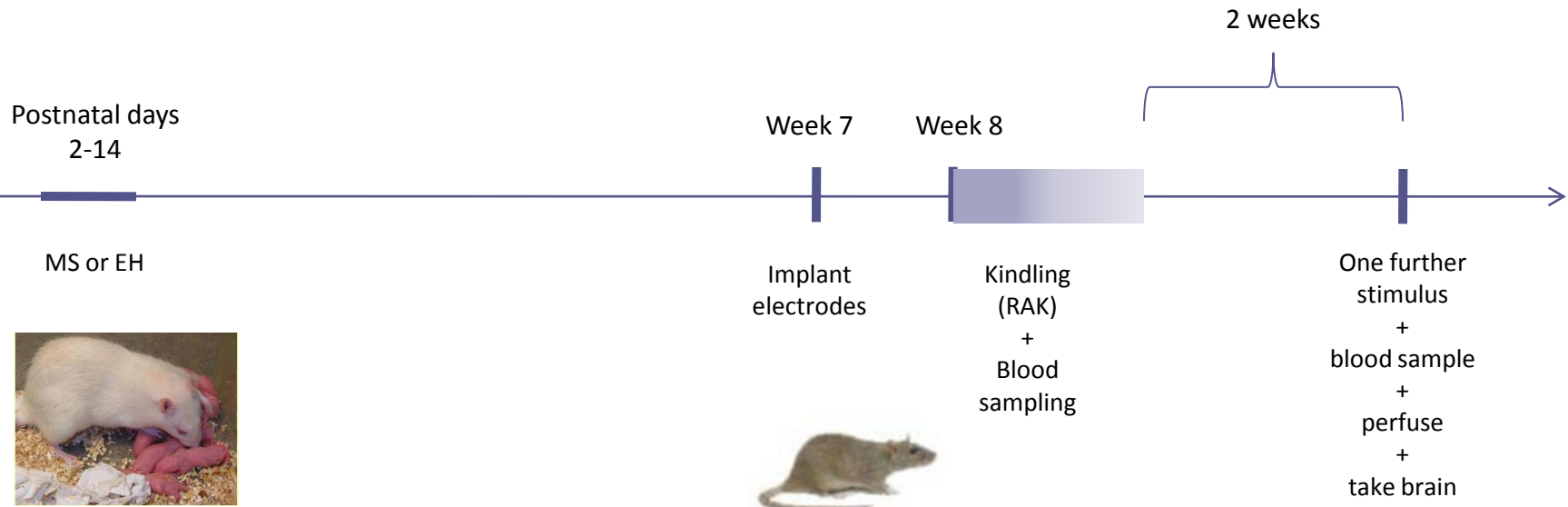
- controls
- 15 mins brief handling & separation each day
- 3 hours separation each day



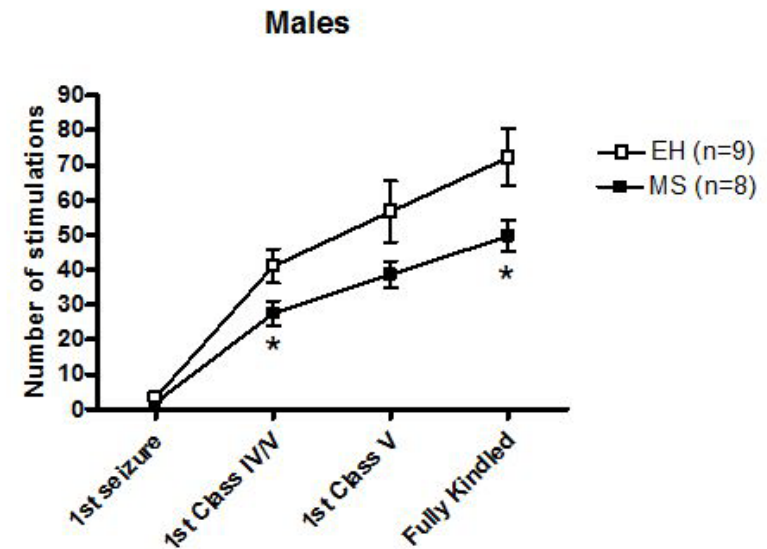
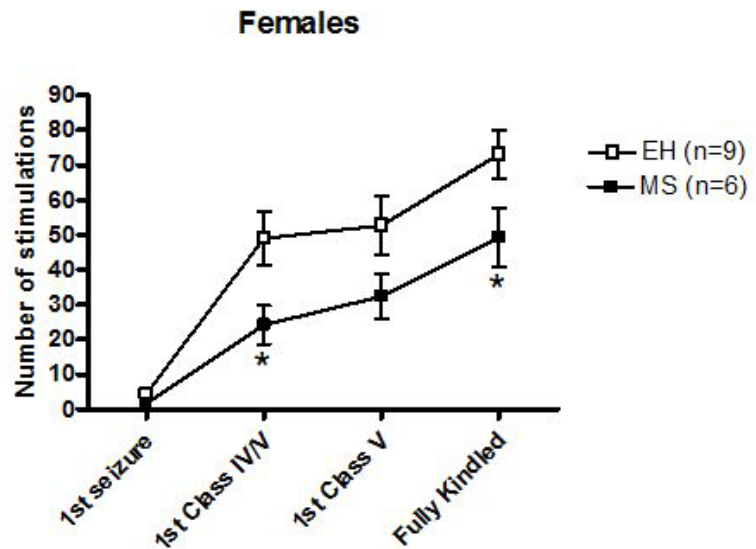
Mirescu et al 2004 *Nature Nsci* 8(7):841-6 **Granule cell layer of dentate gyrus**



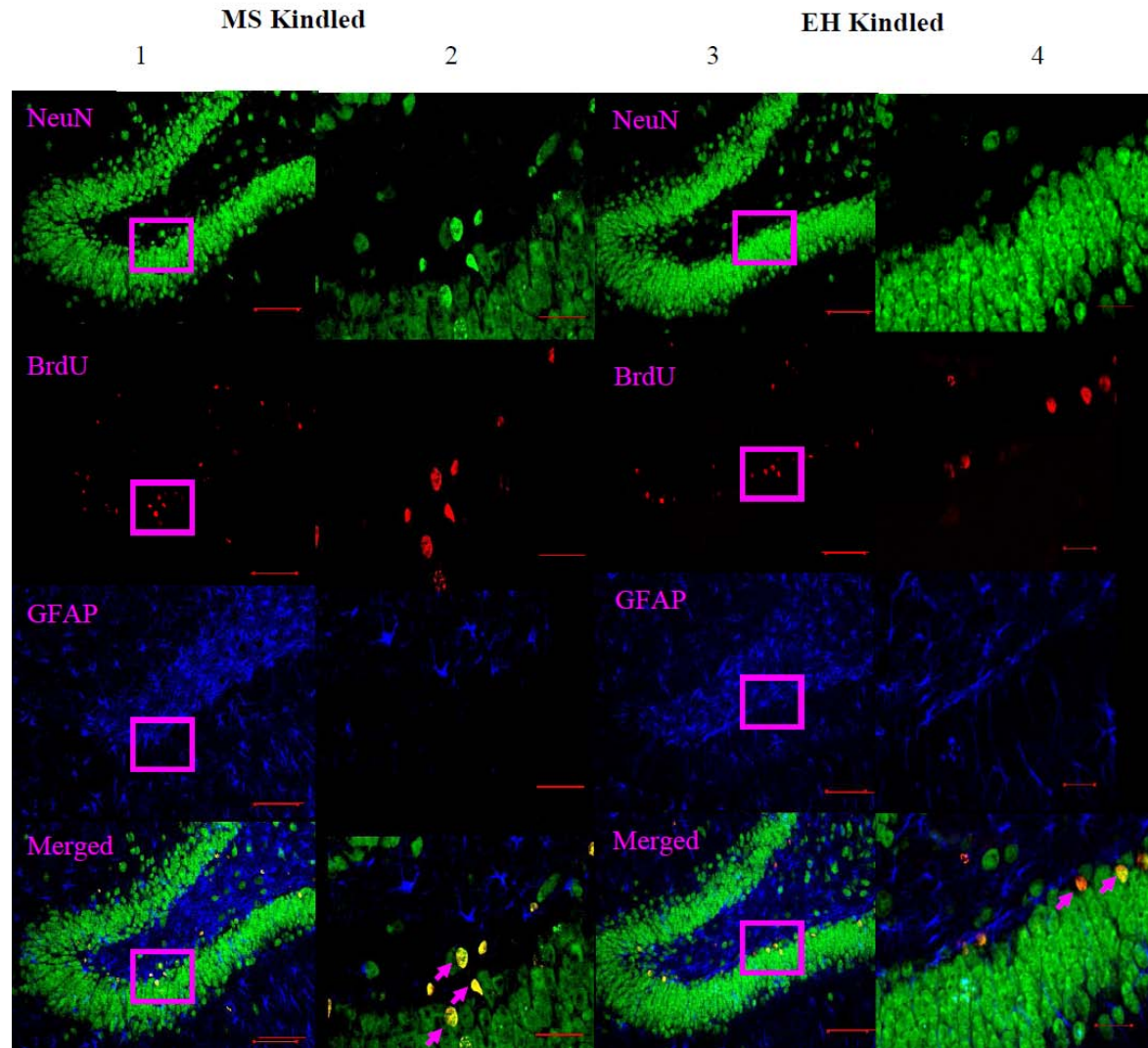
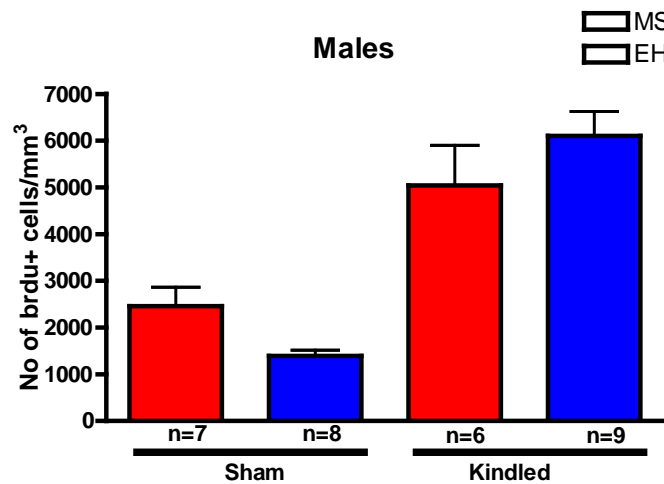
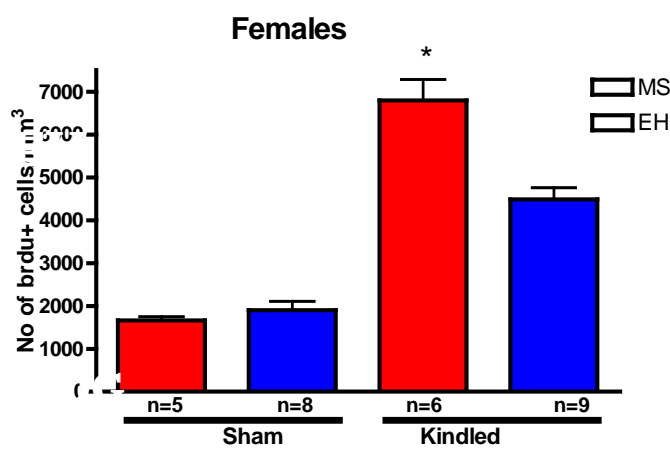
Expt 3: Early life stressor: *daily maternal separation stress*



Rats that had maternal separation stress in early life develop epilepsy much faster



Results: neurogenesis



Females:

Effect of separation: $F=11.27$, $p=0.002$

Effect of kindling: $F=157.41$, $p<0.0001$

Males:

Effect of separation: $F=0.0009$, $p=0.91$

Effect of kindling: $F=37.28$, $p<0.00001$

Key points

- **Many of the factors that cause depression in general population are just as relevant in people with epilepsy**
- **In addition:**
 - The brain epilepsy process itself can contribute
 - There are probably shared brain processes that lead to both epilepsy & depression
 - Depression may aggravate the epilepsy process (?)
- **Important treatment possibilities**
 - Treatment that target the stress system may benefit some epilepsies
 - Treating comorbid depression may have benefits for some epilepsies

5. What can be done about depression in epilepsy?

→ **Dr Simon Jones**

- **Treatment**
- **Prevention**

Psychological/psychiatric services routinely integrated with epilepsy clinical practice and services

Integrated=

- Routine part of comprehensive epilepsy care,

or

- Closely linked

An issue for planning, advocacy, resource allocation/budgets, research

