ADULT HIPPOCAMPAL NEUROGENESIS AND MENTAL HEALTH: THE NEURAL SYMBIOSIS

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Figura 1. Fotografias de Camillo Golgi (1843-1926), à esquerda, e de Santiago Ramón y Cajal (1852-1934), à direita, obtidas no *site* da Fundação Prêmio Nobel (http://nobelprize.org/nobel_prizes/medicine/laureates/1906/).

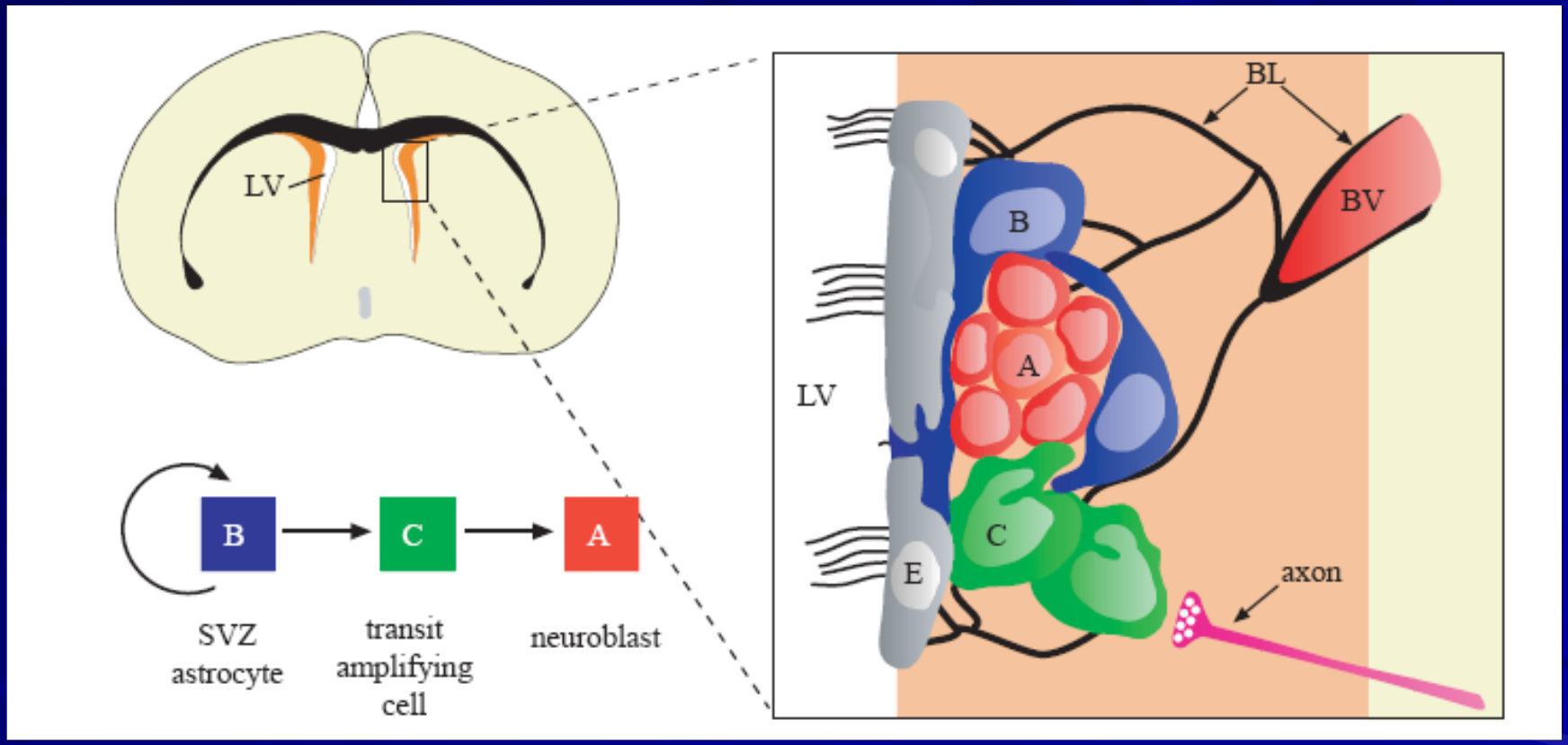
"Once development was ended, the fonts of growth and regeneration of the axons and dendrites dried up irrevocably. In the adult centers, the nerve paths are something fixed, and immutable: everything may die, nothing may be regenerated." Santiago Ramon y Cajal (1).

Ramon y Cajal S. 1928. *Degeneration and Regeneration of the Nervous System*. New York: Hafner

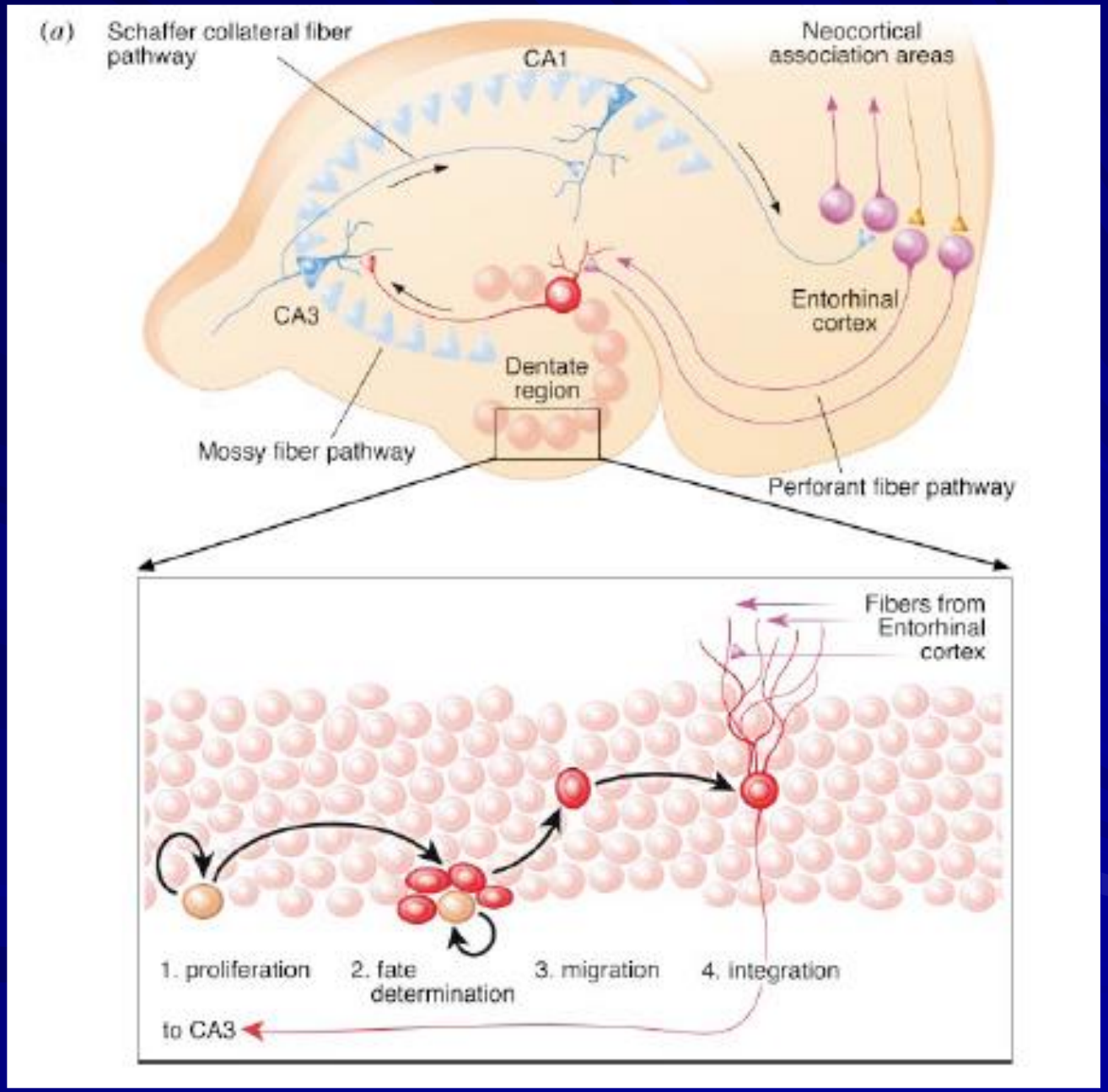
Altman, J. and Das, G.D. (1965) Postnatal origin of microneurons in the rat brain. *Nature* 207, 953–956

Altman, J. and Das, G.D. (1965) Autoradiographic and histological evidence of postnatal hoppocampal neurogenesis in rats. *J. Comp.*

NEW NEURONS ARE PRODUCED IN SPECIFIC BRAIN REGIONS



Riquelme et al., 2007



Lie et al., 2004

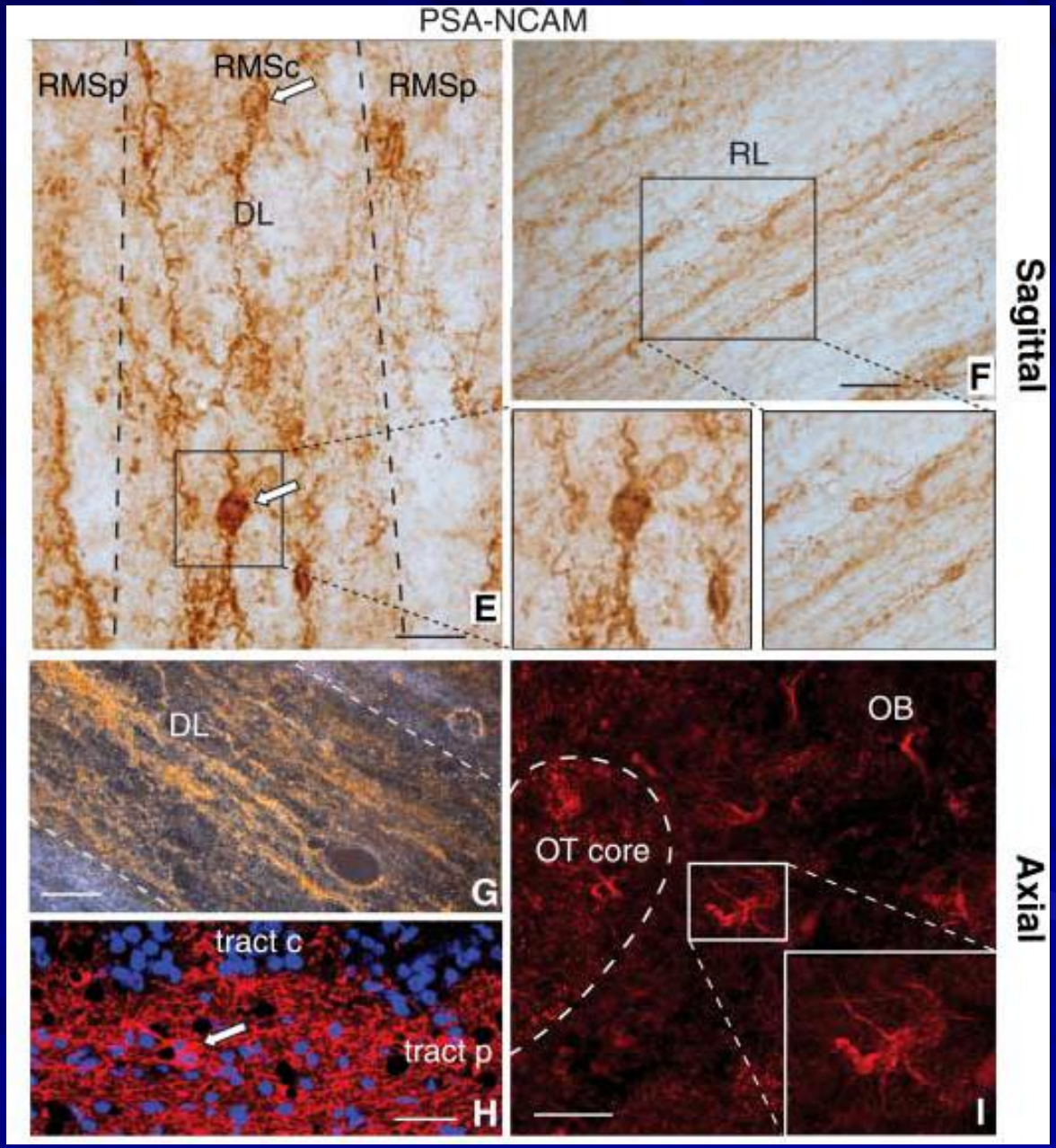
NEUROGENESIS IN THE ADULT HUMAN BRAIN

SUBVENTRICULAR ZONE

Human Neuroblasts Migrate to the Olfactory Bulb via a Lateral Ventricular Extension

Maurice A. Curtis,[1,2] Monica Kam,[1] Ulf Nannmark,[3] Michelle F. Anderson,[2] Mathilda Zetterstrom Axell,[2] Carsten Wikkelso,[2] Stig Holtås,[4] Willeke M. C. van Roon-Mom,[1] Thomas Björk-Eriksson,[5] Claes Nordborg,[6] Jonas Frisén,[7] Michael Dragunow,[8] Richard L. M. Faull,[1]* Peter S. Eriksson[2]*

SCIENCE VOL 315 2 MARCH 2007



Curtis et al., 2007

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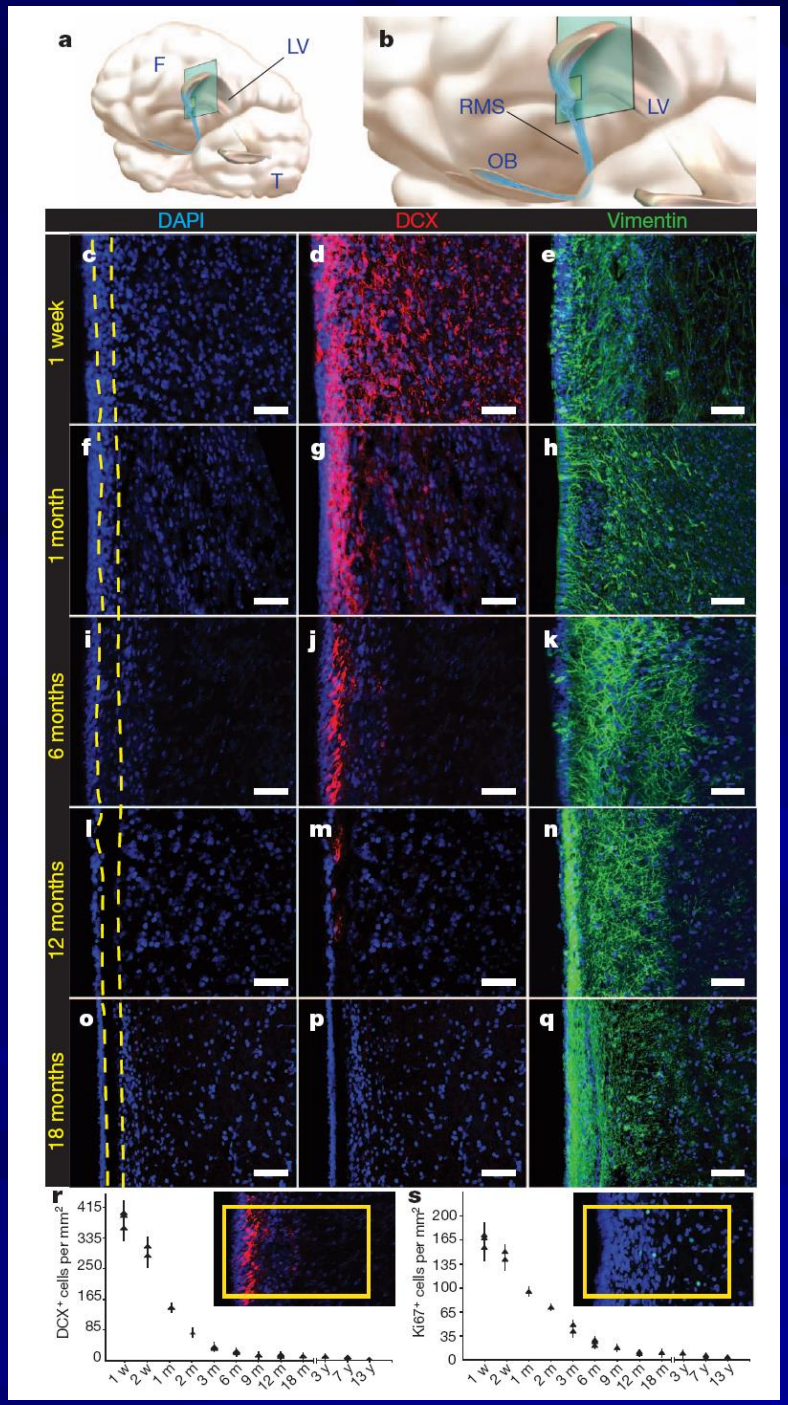
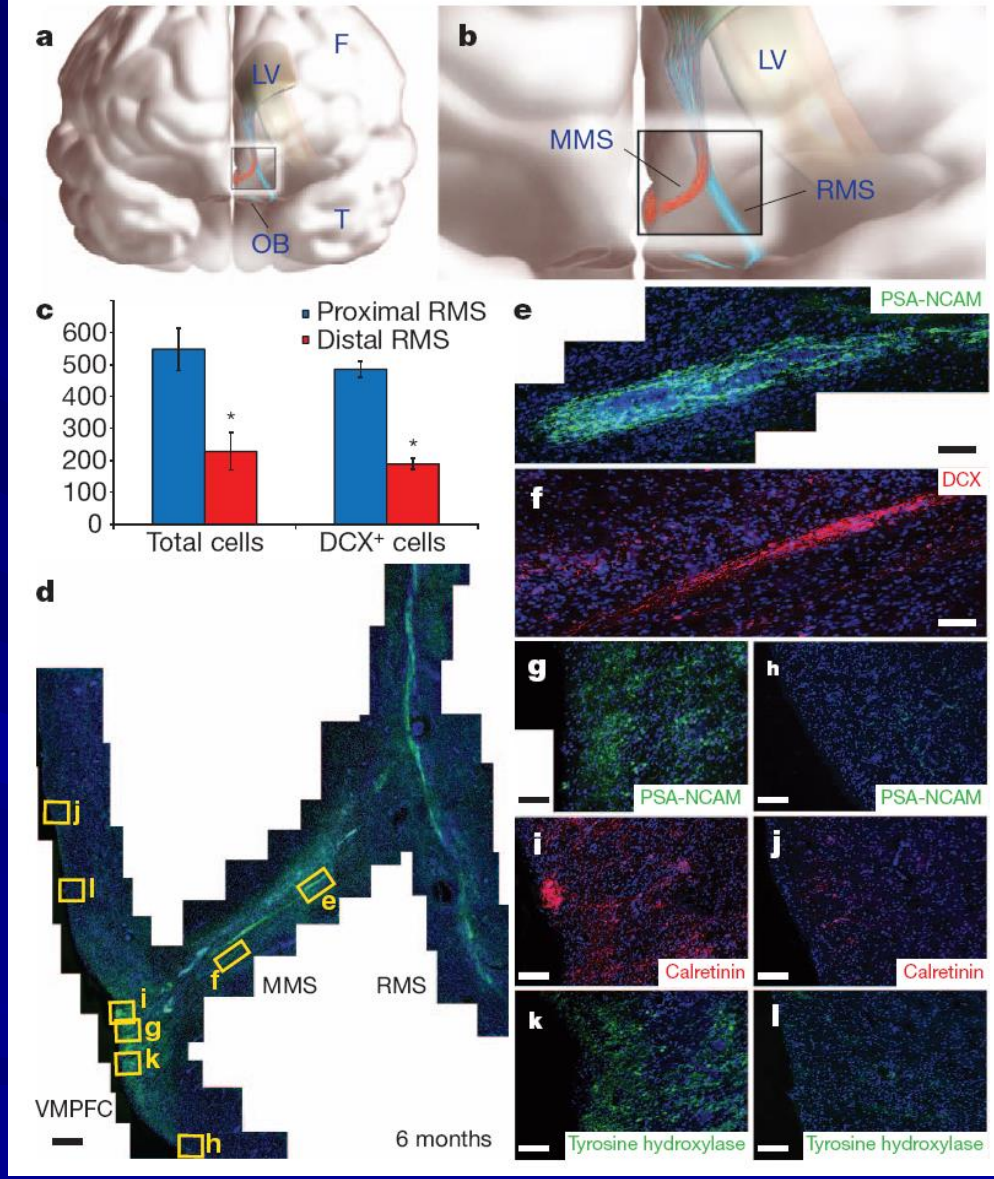
Human hippocampal neurogenesis drops sharply in children to undetectable levels in adults

Shawn F. Sorrells[1,2,*], **Mercedes F. Paredes**[1,3,*], **Arantxa Cebrian-Silla**[4], **Kadellyn Sandoval**[1,3], **Dashi Qi**[5], **Kevin W. Kelley**[1], **David James**[1], **Simone Mayer**[1,3], **Julia Chang**[6], **Kurtis I. Auguste**[2], **Edward Chang**[2], **Antonio J. Gutierrez Martin**[7], **Arnold R. Kriegstein**[1,3], **Gary W. Mathern**[8], **Michael C. Oldham**[1,2], **Eric J. Huang**[9], **Jose Manuel Garcia-Verdugo**[4], **Zhengang Yang**[5], and **Arturo Alvarez-Buylla**[1,2]

[1]Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, University of California San Francisco, California 94143, USA

[2]Department of Neurological Surgery, University of California San Francisco, California 94143, USA


a
F
LV
T
b
RMS
LV
OB
DAPI
DCX
Vimentin
1 week
1 month
6 months
12 months
18 months
c
d
e
f
g
h
i
j
k
l
m
n
o
p
q
r
DCX+ cells per mm2
415
335
250
165
85
0
1 w
2 w
1 m
2 m
3 m
6 m
9 m
12 m
18 m
3 y
7 y
13 y
s
Ki67+ cells per mm2
200
165
135
100
65
35
0


a
F
LV
OB
T
b
LV
MMS
RMS
c
Proximal RMS
Distal RMS
600
500
400
300
200
100
0
Total cells
DCX+ cells
d
j
l
e
f
MMS
RMS
i
g
k
VMPFC
h
6 months
e
PSA-NCAM
f
DCX
g
PSA-NCAM
h
PSA-NCAM
i
Calretinin
j
Calretinin
k
Tyrosine hydroxylase
l
Tyrosine hydroxylase

HIPPOCAMPUS

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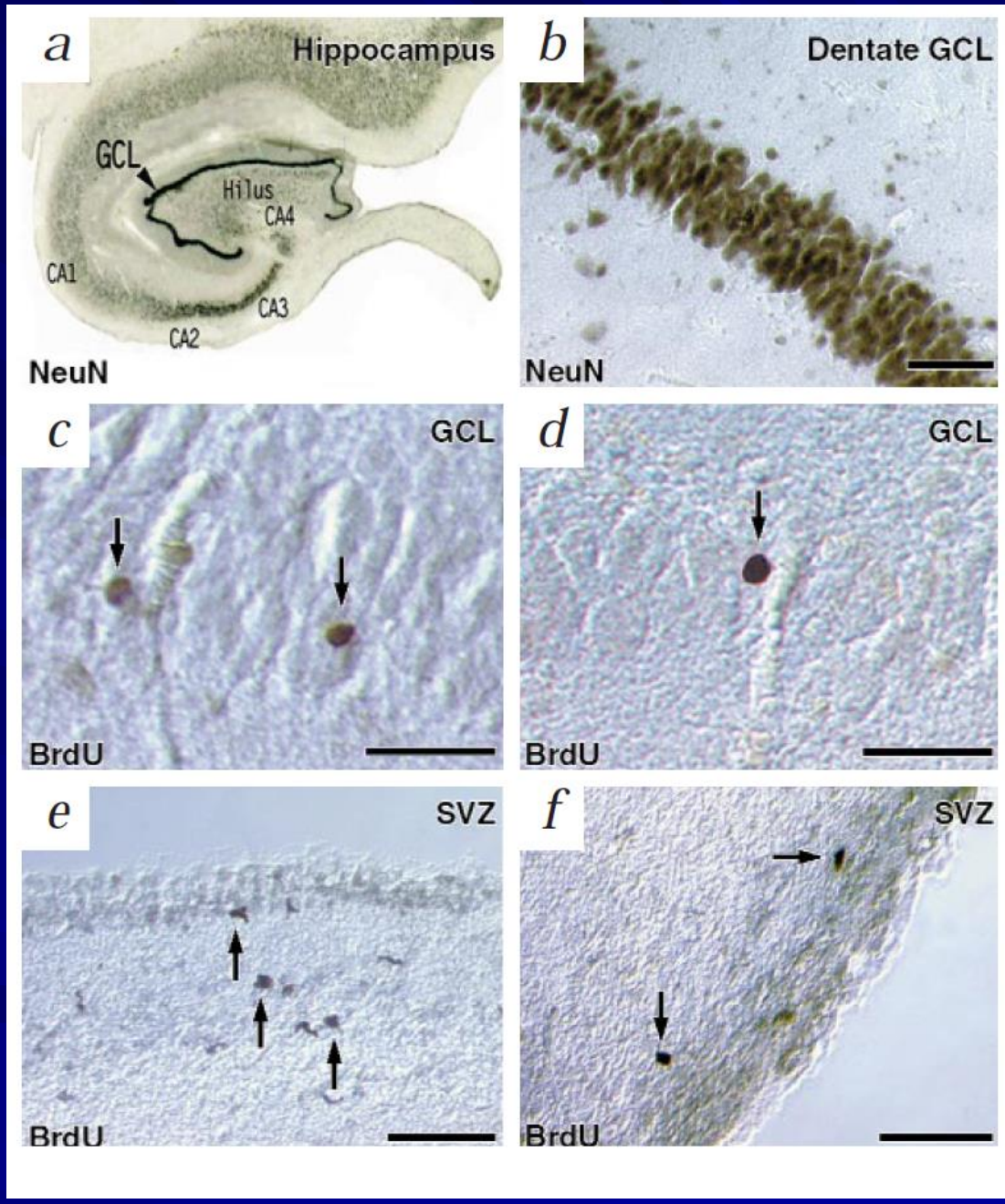
Neurogenesis in the adult human hippocampus

PETER S. ERIKSSON[1,4], EKATERINA PERFILIEVA[1], THOMAS BJÖRK-ERIKSSON[2], ANN-MARIE ALBORN[1], CLAES NORDBORG[3], DANIEL A. PETERSON[4] & FRED H. GAGE[4]

Department of Clinical Neuroscience, Institute of Neurology[1], Department of Oncology[2], Department of Pathology[3], Sahlgrenska University Hospital, 41345 Göteborg, Sweden

[4]Laboratory of Genetics, The Salk Institute for Biological Studies, 10010 North Torrey Pines Road, La Jolla, California 92037, USA

Correspondence should be addressed to F.H.G.


a
Hippocampus
GCL
Hilus
CA4
CA1
CA3
CA2
NeuN
b
Dentate GCL
NeuN
c
GCL
BrdU
d
GCL
BrdU
e
SVZ
BrdU
f
SVZ
BrdU

HHS Public Access

Author manuscript

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Dynamics of hippocampal neurogenesis in adult humans

Kirsty L. Spalding[#1], **Olaf Bergmann**[#1], **Kanar Alkass**[1,2], **Samuel Bernard**[3], **Mehran Salehpour**[4], **Hagen B. Huttner**[1,5], **Emil Boström**[1], **Isabelle Westerlund**[1], **Celine Vial**[3], **Bruce A. Buchholz**[6], **Göran Possnert**[4], **Deborah C. Mash**[7], **Henrik Druid**[2], and **Jonas Frisén**[1]

[1]Department of Cell and Molecular Biology, Karolinska Institute, Stockholm, Sweden

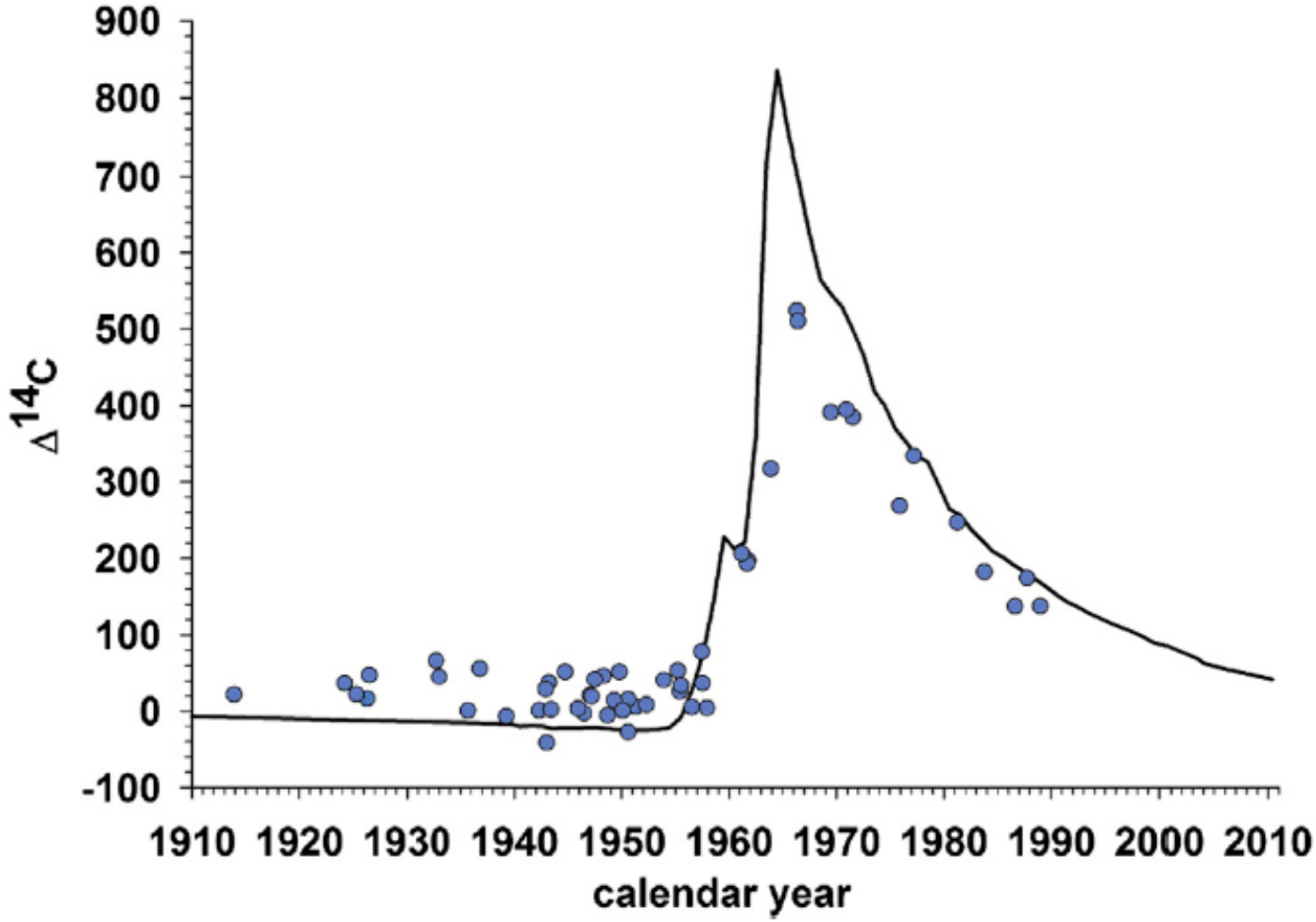

Figure 3. Hippocampal Neurogenesis in Adult Humans

^{14}C concentrations in hippocampal neuron genomic DNA correspond to a time after the date of birth of the individual, demonstrating neurogenesis throughout life.

LETTER

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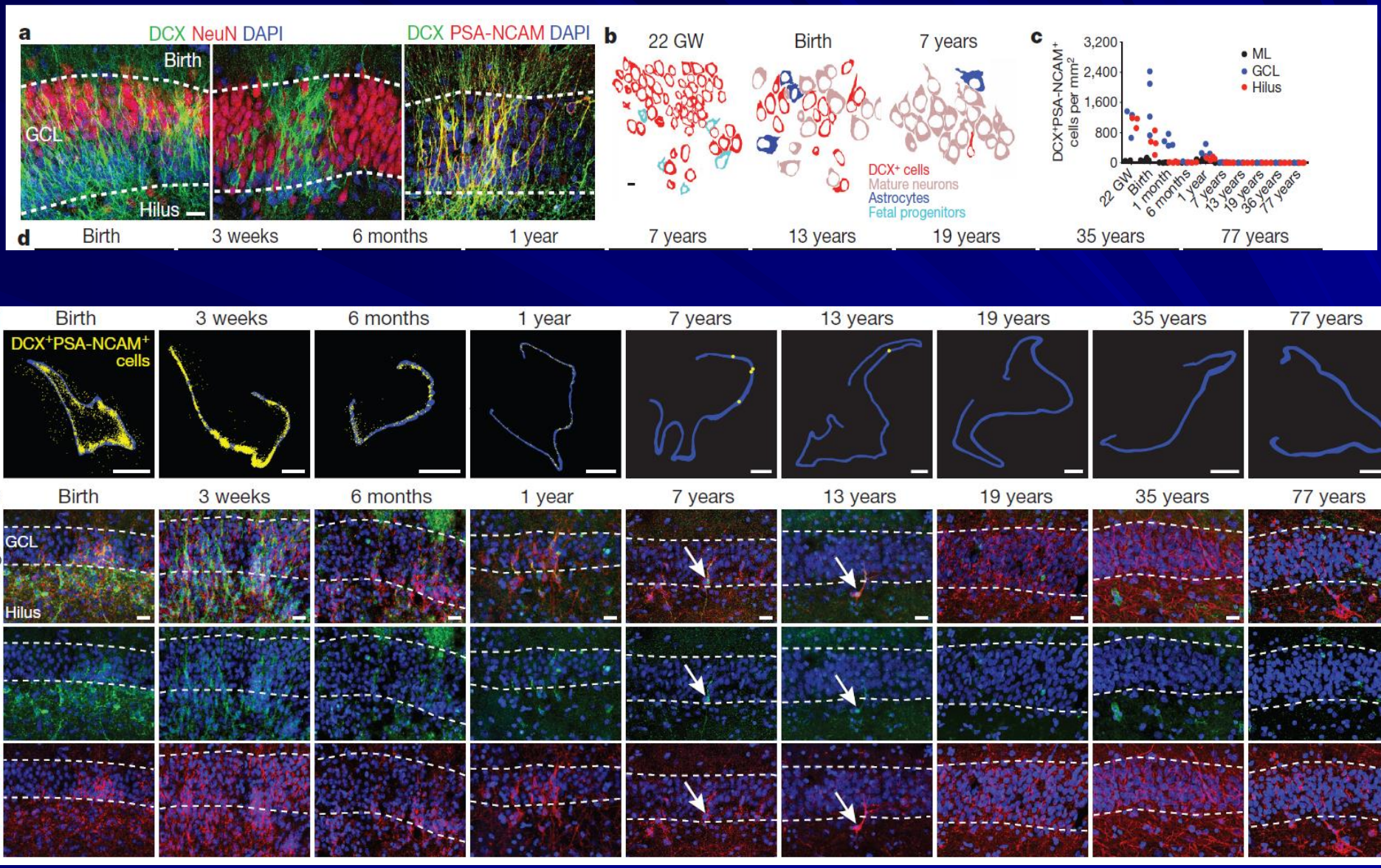
Human hippocampal neurogenesis drops sharply in children to undetectable levels in adults

Shawn F. Sorrells[1,2]*, Mercedes F. Paredes[1,3]*, Arantxa Cebrian-Silla[4], Kadellyn Sandoval[1,3], Dashi Qi[5], Kevin W. Kelley[1], David James[1], Simone Mayer[1,3], Julia Chang[6], Kurtis I. Auguste[2], Edward F. Chang[2], Antonio J. Gutierrez[7], Arnold R. Kriegstein[1,3], Gary W. Mathern[8,9], Michael C. Oldham[1,2], Eric J. Huang[10], Jose Manuel Garcia-Verdugo[4], Zhengang Yang[5] & Arturo Alvarez-Buylla[1,2]


a
DCX NeuN DAPI
DCX PSA-NCAM DAPI
Birth
GCL
Hilus
b
22 GW
Birth
7 years
DCX+ cells
Mature neurons
Astrocytes
Fetal progenitors
c
DCX+PSA-NCAM+ cells per mm2
3,200
2,400
1,600
800
0
ML
GCL
Hilus
22 GW
Birth
1 month
6 months
1 year
7 years
13 years
19 years
36 years
77 years
d
Birth
3 weeks
6 months
1 year
7 years
13 years
19 years
35 years
77 years
DCX+PSA-NCAM+ cells
e
Merge
DCX
PSA-NCAM
GCL
Hilus

Cell Stem Cell
Short Article

Human Hippocampal Neurogenesis Persists throughout Aging

Maura Boldrini,[1,5,9,10,*] Camille A. Fulmore,[5] Alexandria N. Tartt,[5] Laika R. Simeon,[5] Ina Pavlova,[6] Verica Poposka,[8] Gorazd B. Rosoklija,[1,5,7] Aleksandar Stankov,[8] Victoria Arango,[1,5] Andrew J. Dwork,[1,2,5,7] René Hen,[1,3,4,6] and J. John Mann[1,5]

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[4]Department of Pharmacology, Columbia University, New York, NY 10032, USA
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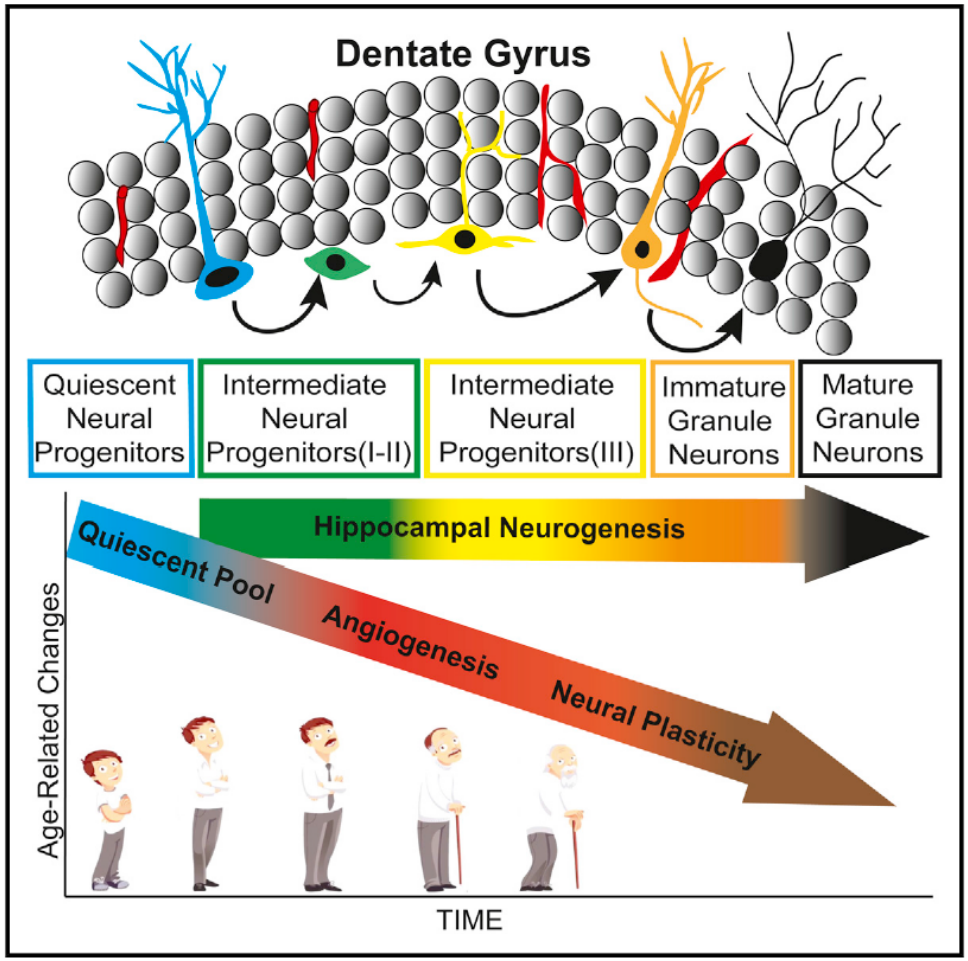
https://doi.org/10.1016/j.stem.2018.03.015

Cell Stem Cell

Human Hippocampal Neurogenesis Persists throughout Aging

Graphical Abstract



Authors

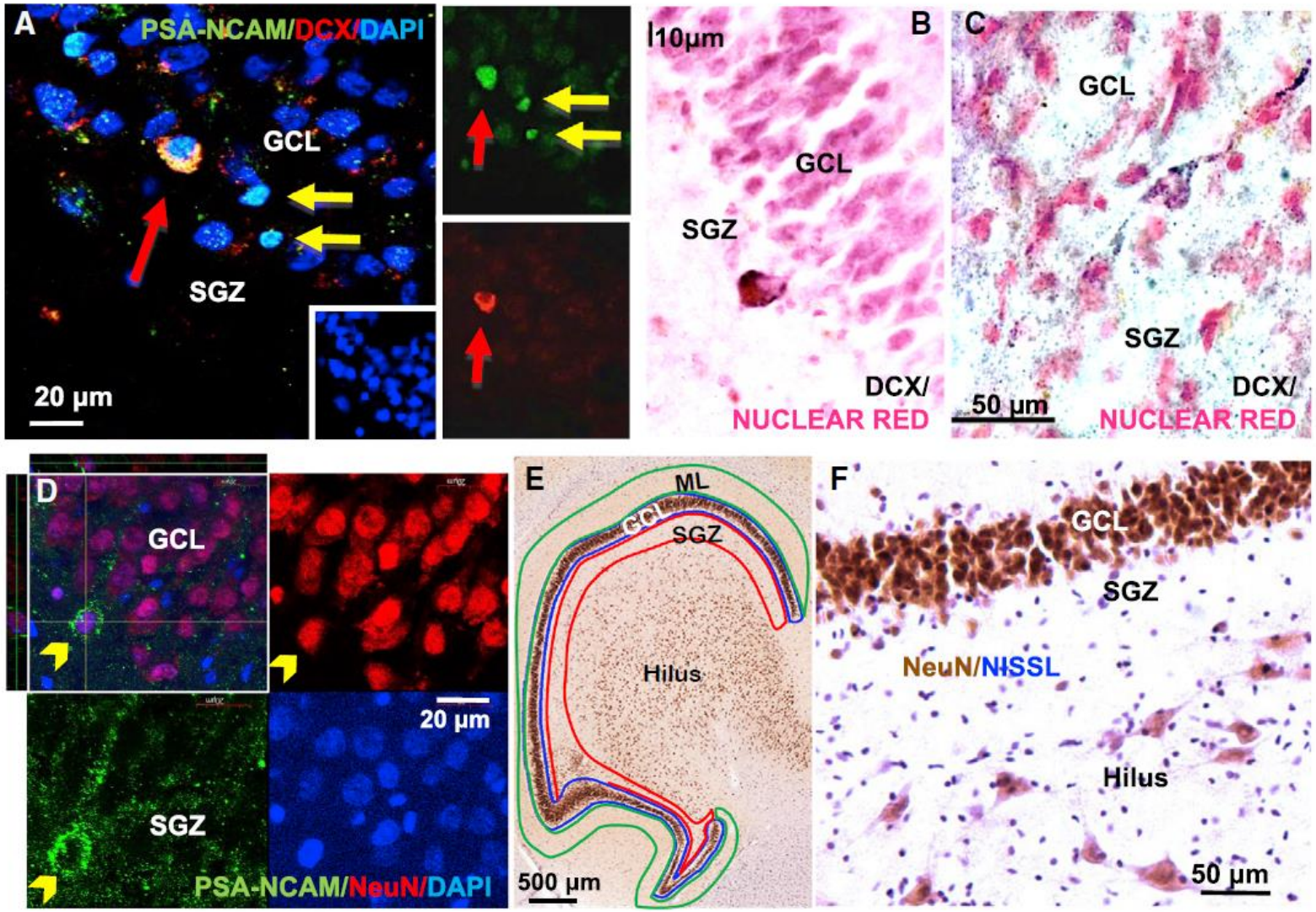
Maura Boldrini, Camille A. Fulmore, Alexandria N. Tartt, ..., Andrew J. Dwork, René Hen, J. John Mann

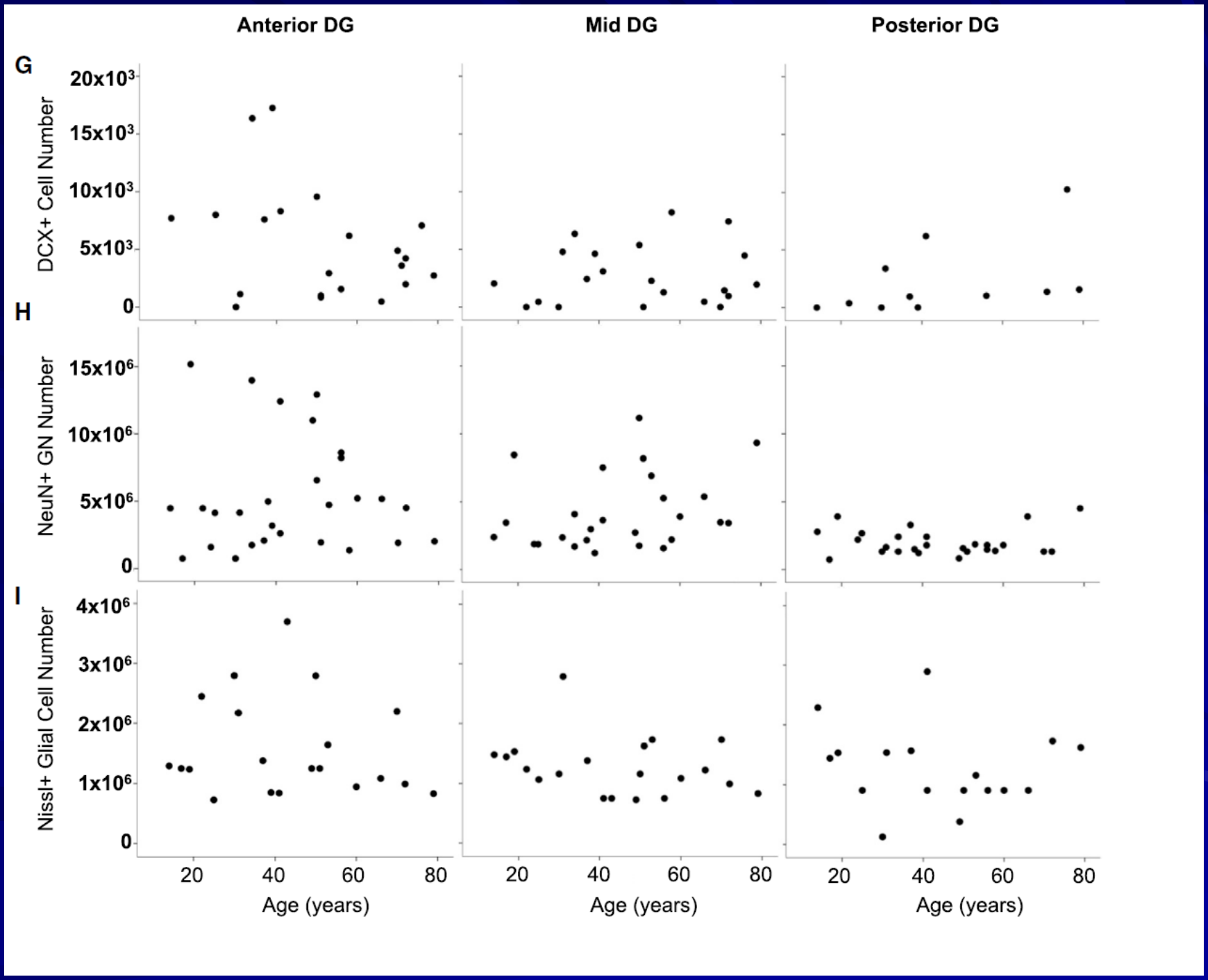
Correspondence

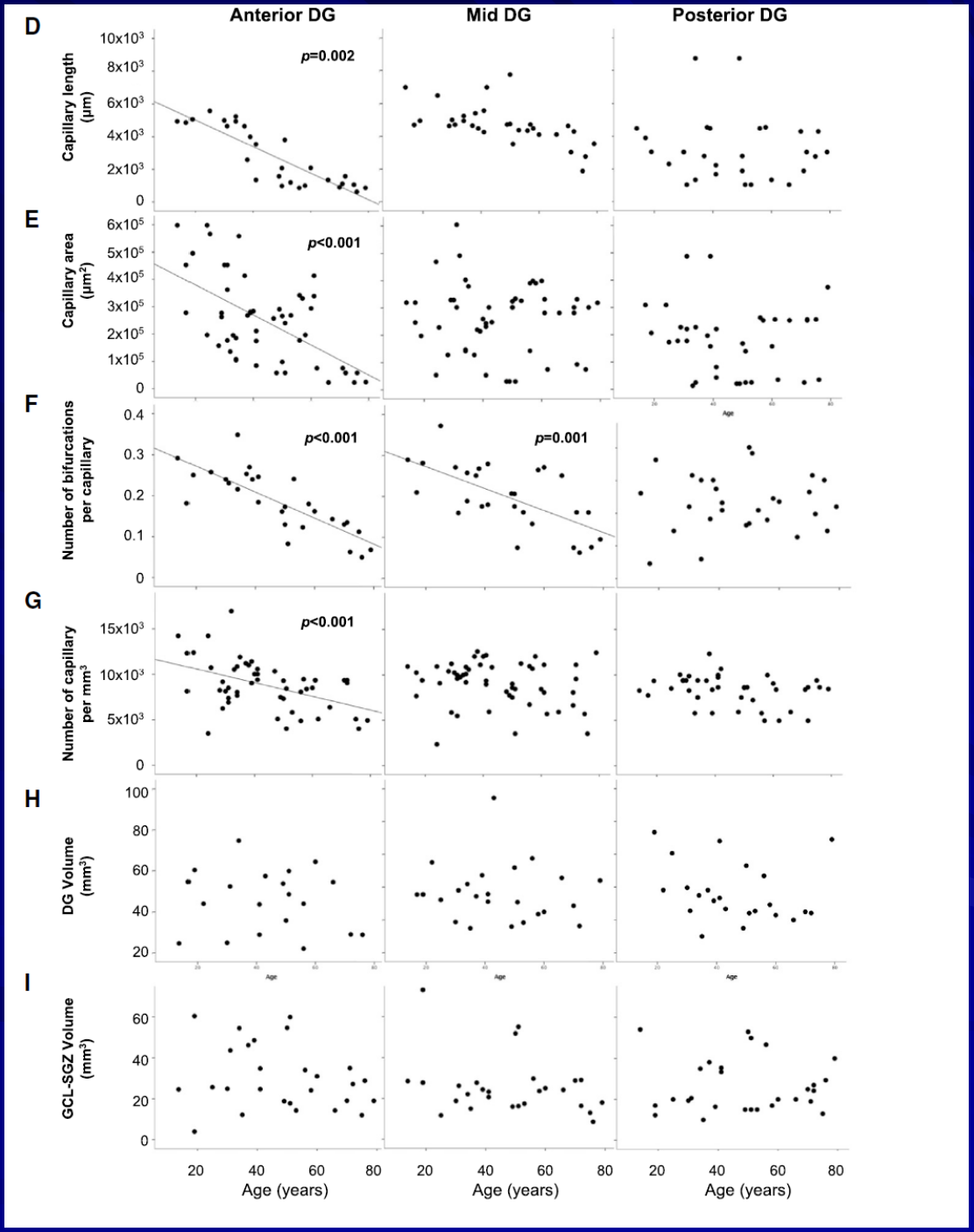
mb928@cumc.columbia.edu

In Brief

Boldrini et al. find persistent adult neurogenesis in humans into the eighth decade of life, despite declines in quiescent stem cell pools, angiogenesis, and neuroplasticity. Over a 65-year age span, proliferating neural progenitors, immature and mature granule neurons, glia, and dentate gryus volume were unchanged.


A
PSA-NCAM/DCX/DAPI
GCL
SGZ
20 μm
B
10μm
GCL
SGZ
DCX/
NUCLEAR RED
C
GCL
SGZ
50 μm
DCX/
NUCLEAR RED
D
GCL
SGZ
20 μm
PSA-NCAM/NeuN/DAPI
E
ML
GCL
SGZ
Hilus
500 μm
F
GCL
SGZ
NeuN/NISSL
Hilus
50 μm
Anterior DG
Mid DG
Posterior DG


Anterior DG
Mid DG
Posterior DG
G
DCX+ Cell Number
20x10³
15x10³
10x10³
5x10³
0
H
NeuN+ GN Number
15x10⁶
10x10⁶
5x10⁶
0
I
Nissl+ Glial Cell Number
4x10⁶
3x10⁶
2x10⁶
1x10⁶
0
20
40
60
80
Age (years)


D
Anterior DG
Mid DG
Posterior DG
Capillary length (µm)
p=0.002
E
Capillary area (µm²)
p<0.001
F
Number of bifurcations per capillary
p<0.001
p=0.001
G
Number of capillary per mm³
p<0.001
H
DG Volume (mm³)
I
GCL-SGZ Volume (mm³)
Age (years)
Age (years)
Age (years)

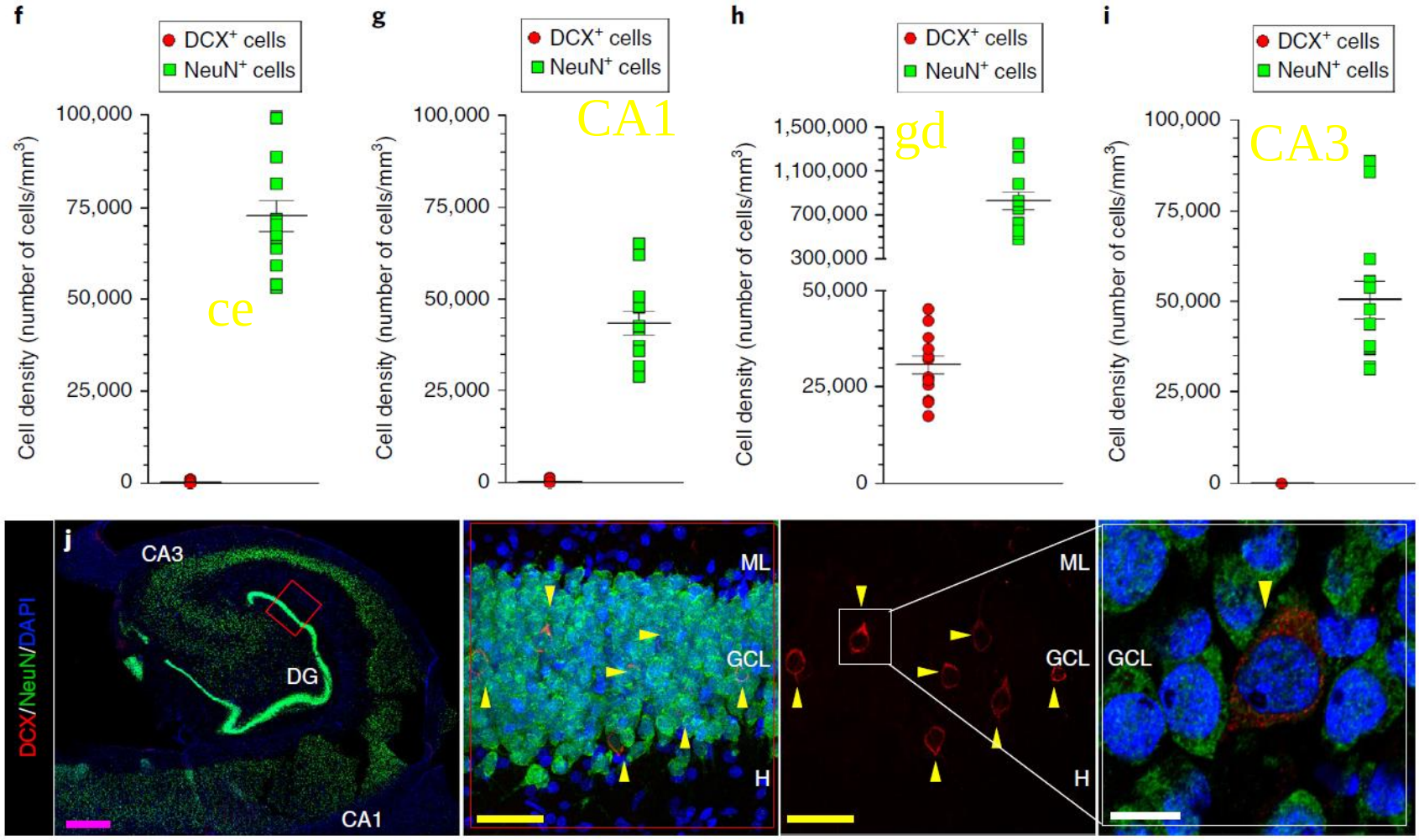
nature medicine

LETTERS

https://doi.org/10.1038/s41591-019-0375-9

Adult hippocampal neurogenesis is abundant in neurologically healthy subjects and drops sharply in patients with Alzheimer's disease

Elena P. Moreno-Jiménez[1,2,3,6], Miguel Flor-García[1,2,3,6], Julia Terreros-Roncal[1,2,3,6], Alberto Rábano[4], Fabio Cafini[5], Noemí Pallas-Bazarra[1,3], Jesús Ávila[1,3] and María Llorens-Martín[1,2,3*]


f
DCX+ cells
NeuN+ cells
Cell density (number of cells/mm3)
100,000
75,000
50,000
25,000
0
ce
g
DCX+ cells
NeuN+ cells
Cell density (number of cells/mm3)
100,000
75,000
50,000
25,000
0
CA1
h
DCX+ cells
NeuN+ cells
Cell density (number of cells/mm3)
1,500,000
1,100,000
700,000
300,000
50,000
25,000
0
gd
i
DCX+ cells
NeuN+ cells
Cell density (number of cells/mm3)
100,000
75,000
50,000
25,000
0
CA3
j
DCX/NeuN/DAPI
CA3
DG
CA1
ML
GCL
H
ML
GCL
H
GCL

ESTRIADO

Cell

Neurogenesis in the Striatum of the Adult Human Brain

Aurélie Ernst,[1] Kanar Alkass,[1,2] Samuel Bernard,[3] Mehran Salehpour,[4] Shira Perl,[5] John Tisdale,[5] Göran Possnert,[4] Henrik Druid,[2] and Jonas Frisén[1,*]
[1]Department of Cell and Molecular Biology
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http://dx.doi.org/10.1016/j.cell.2014.01.044

FUNÇÕES DA NEUROGÊNESE ADULTA

RESERVE OF NEURONS FOR TISSUE REPAIR

Neuronal replacement from endogenous precursors in the adult brain after stroke

ANDREAS ARVIDSSON[1], TOVE COLLIN[1], DENIZ KIRIK[2], ZAAL KOKAIA[1] & OLLE LINDVALL[1]

[1]Section of Restorative Neurology and [2]Neurobiology, Wallenberg Neuroscience Center, Lund University Hospital, Lund, Sweden
Correspondence should be addressed to A.A.; email: andreas.arvidsson@neurol.lu.se
Z.K. and O.L. contributed equally to this study.

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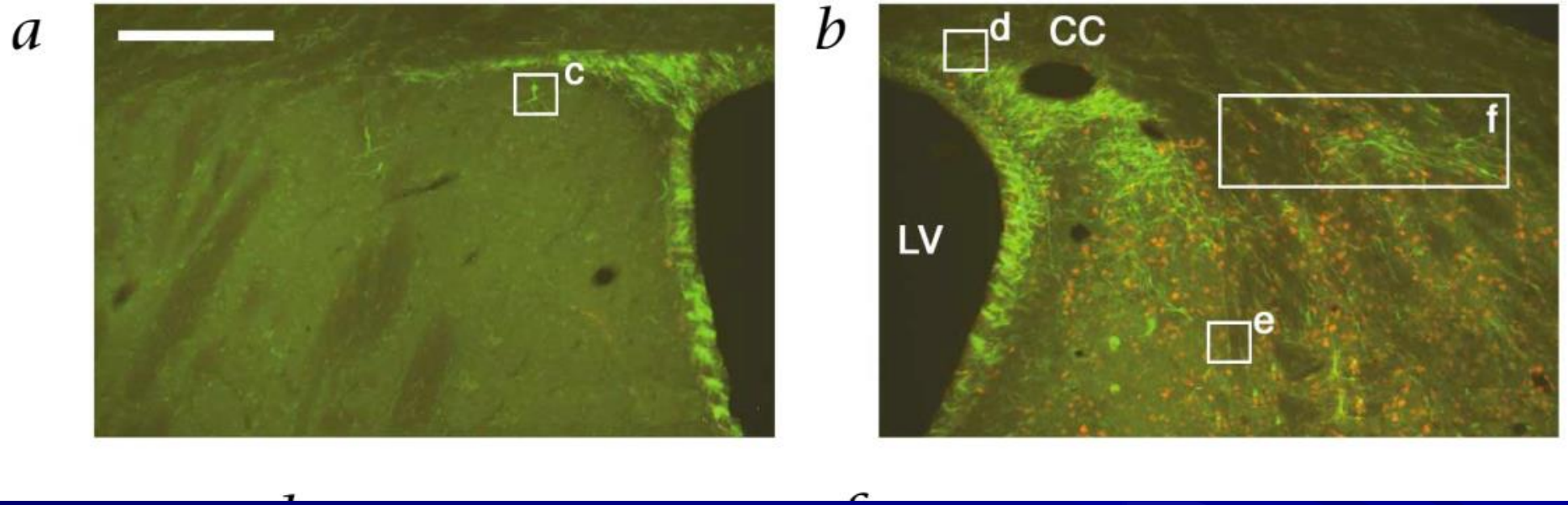
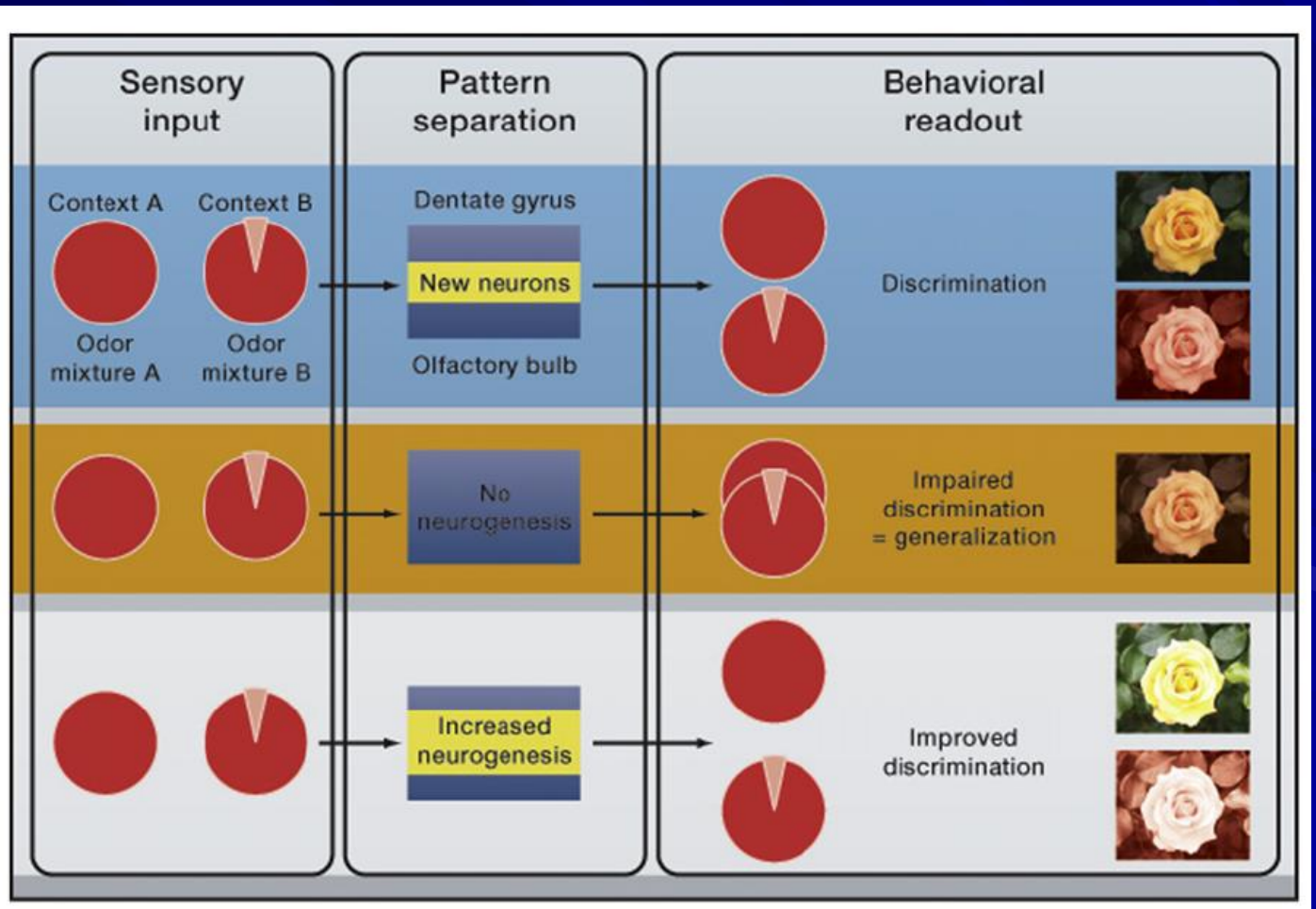

a
c
b
d
CC
f
LV
e

Pattern Separation: A Common Function for New Neurons in Hippocampus and Olfactory Bulb

Amar Sahay,[1,2] Donald A. Wilson,[3] and René Hen[1,2,*]
[1]Departments of Neuroscience and Psychiatry, Columbia University, New York, NY 10032, USA
[2]Division of Integrative Neuroscience, The New York State Psychiatric Institute, New York, NY 10032, USA
[3]Emotional Brain Institute, Nathan Kline Institute for Psychiatric Research, and Child and Adolescent Psychiatry, New York University School of Medicine, Orangeburg, New York, NY 10962, USA
*Correspondence: rh95@columbia.edu
DOI 10.1016/j.neuron.2011.05.012



ADULT HIPPOCAMPAL NEUROGENESIS AND AFFECTIVE DISORDERS

HHS Public Access

Author manuscript

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Adult hippocampal neurogenesis and cognitive flexibility — linking memory and mood

Christoph Anacker[1] and **René Hen**[1,2,3]

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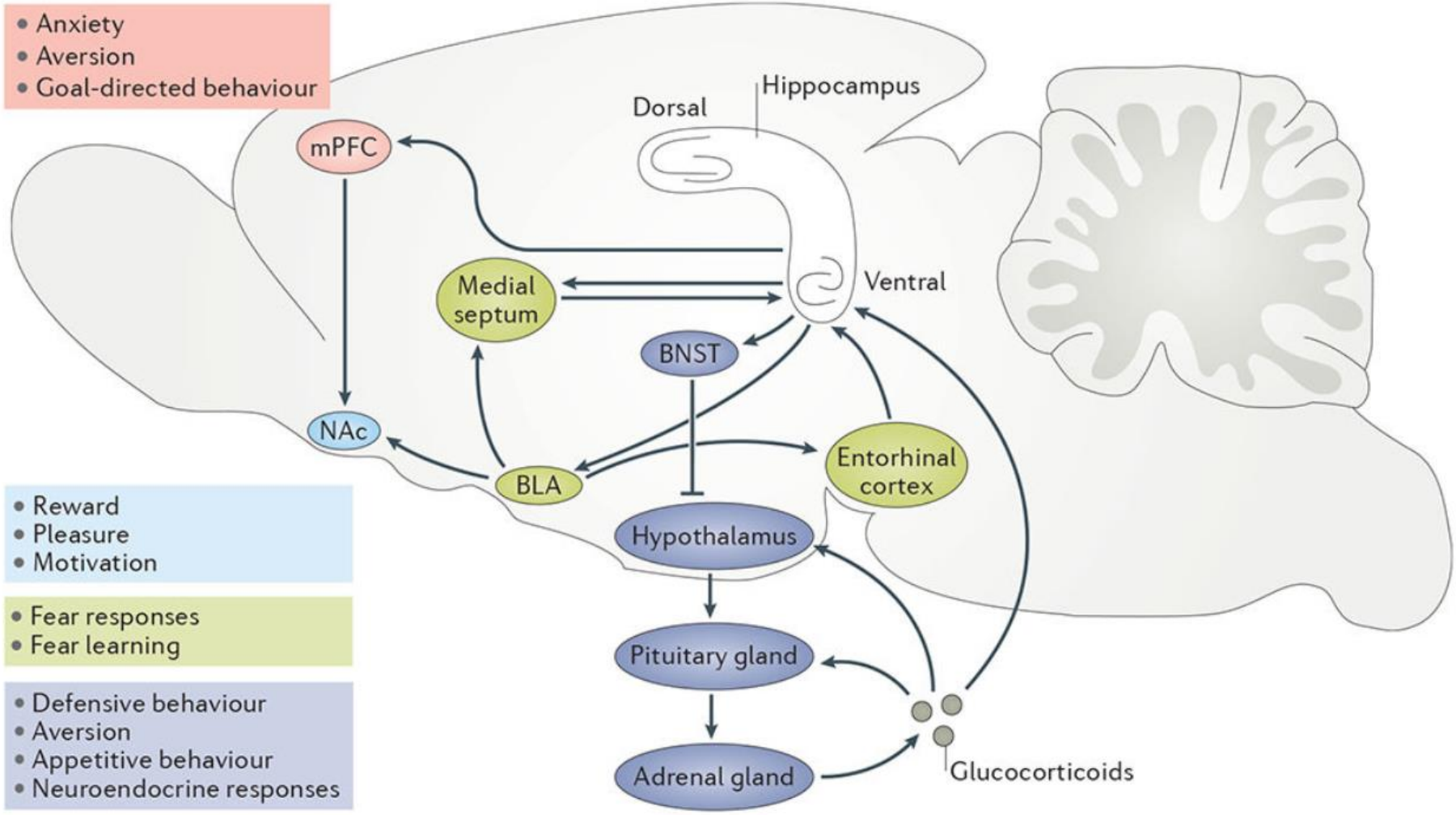
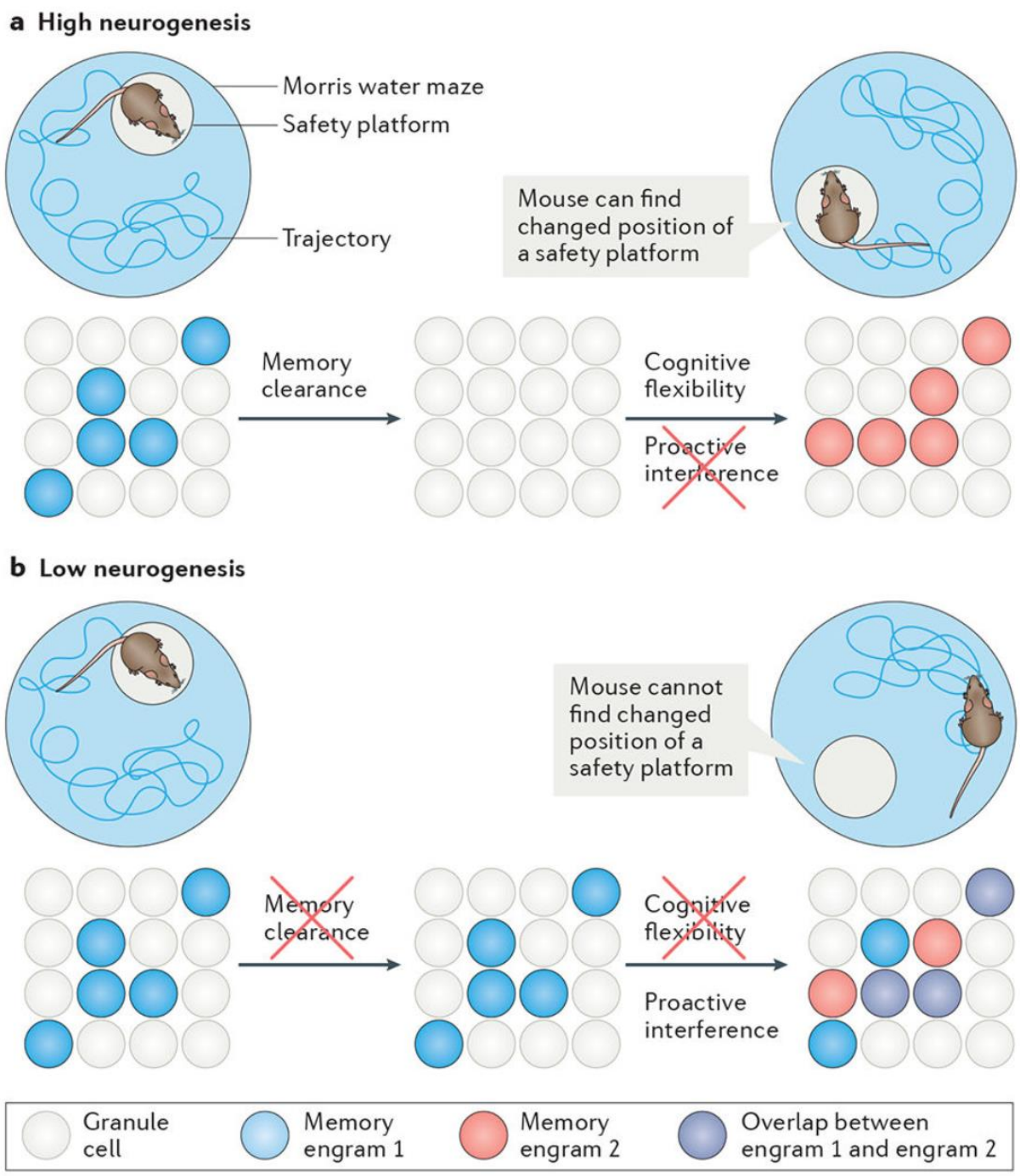

• Anxiety
• Aversion
• Goal-directed behaviour
Dorsal
Hippocampus
mPFC
Medial septum
Ventral
BNST
NAc
BLA
Entorhinal cortex
• Reward
• Pleasure
• Motivation
Hypothalamus
• Fear responses
• Fear learning
Pituitary gland
• Defensive behaviour
• Aversion
• Appetitive behaviour
• Neuroendocrine responses
Adrenal gland
Glucocorticoids


a High neurogenesis
Morris water maze
Safety platform
Trajectory
Mouse can find changed position of a safety platform
Memory clearance
Cognitive flexibility
Proactive interference
b Low neurogenesis
Mouse cannot find changed position of a safety platform
Memory clearance
Cognitive flexibility
Proactive interference
Granule cell
Memory engram 1
Memory engram 2
Overlap between engram 1 and engram 2

HHS Public Access

Author manuscript

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Hippocampal neurogenesis confers stress resilience by inhibiting the ventral dentate gyrus

Christoph Anacker[1,*], **Victor M. Luna**[1], **Gregory Stevens**[1], **Amira Millette**[1], **Ryan Shores**[1], **Jessica C. Jimenez**[1], **Briana Chen**[1], and **René Hen**[1,2,3,*]

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Requirement of Hippocampal Neurogenesis for the Behavioral Effects of Antidepressants

Luca Santarelli,[1*] Michael Saxe,[1*] Cornelius Gross,[1] Alexandre Surget,[2] Fortunato Battaglia,[3] Stephanie Dulawa,[1] Noelia Weisstaub,[1] James Lee,[1] Ronald Duman,[4] Ottavio Arancio,[3] Catherine Belzung,[2] René Hen[1†]

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Antidepressants increase neural progenitor cells in the human hippocampus

Maura Boldrini[1,5,7], **Mark D. Underwood**[1,5], **René Hen**[1,3,4,6], **Gorazd B. Rosoklija**[1,5,8], **Andrew J. Dwork**[1,2,5], **J. John Mann**[1,5], and **Victoria Arango**[1,5]

[1]Department of Psychiatry, Columbia University

[2]Department of Pathology and Cell Biology, Columbia University

AEROBIC EXERCISE INCREASES HIPPOCAMPAL NEUROGENESIS IN RODENTS

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Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus

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[1] *Laboratory of Genetics, The Salk Institute for Biological Studies, 10010 N. Torrey Pines Road, La Jolla, California 92037, USA*

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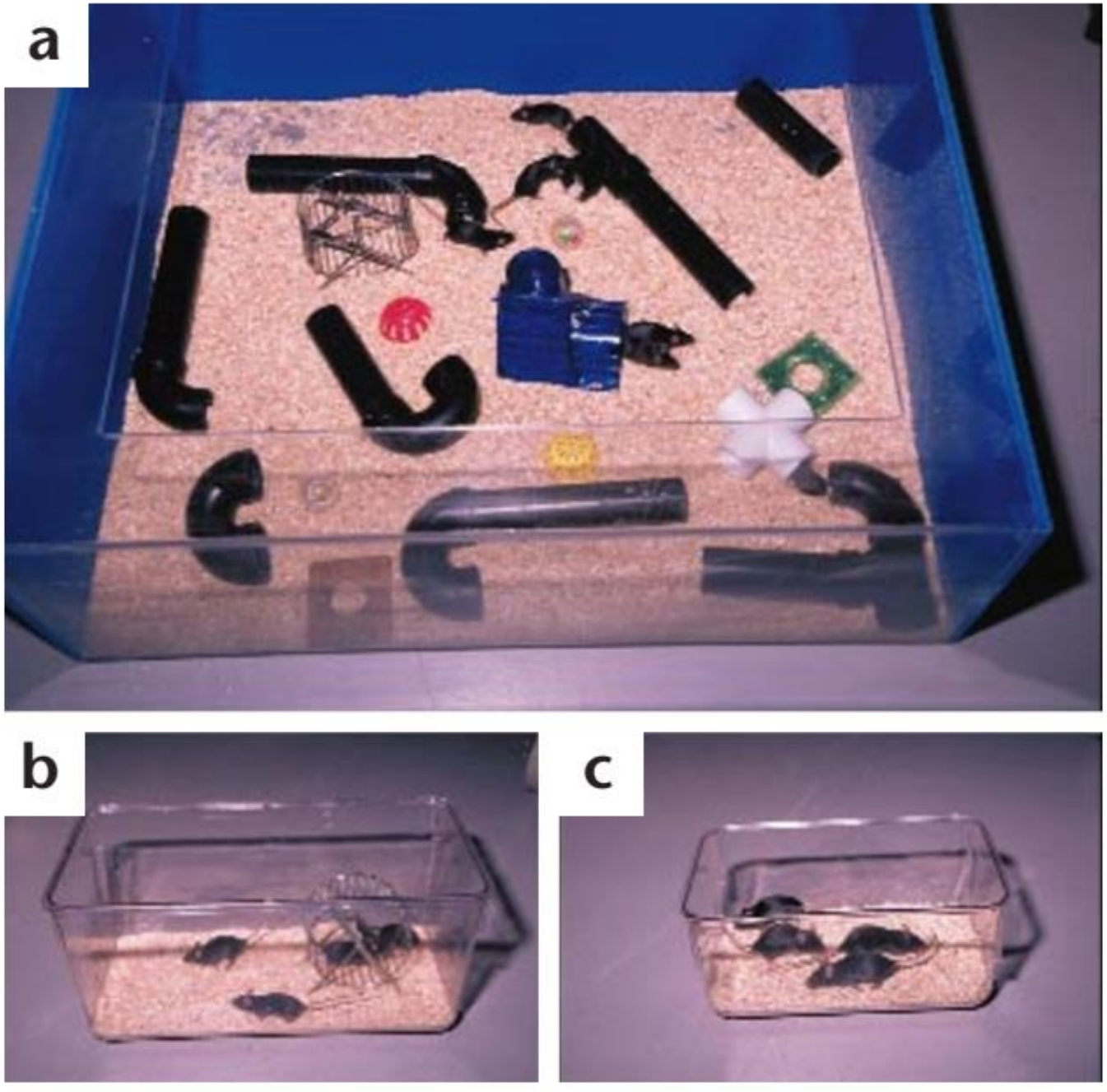
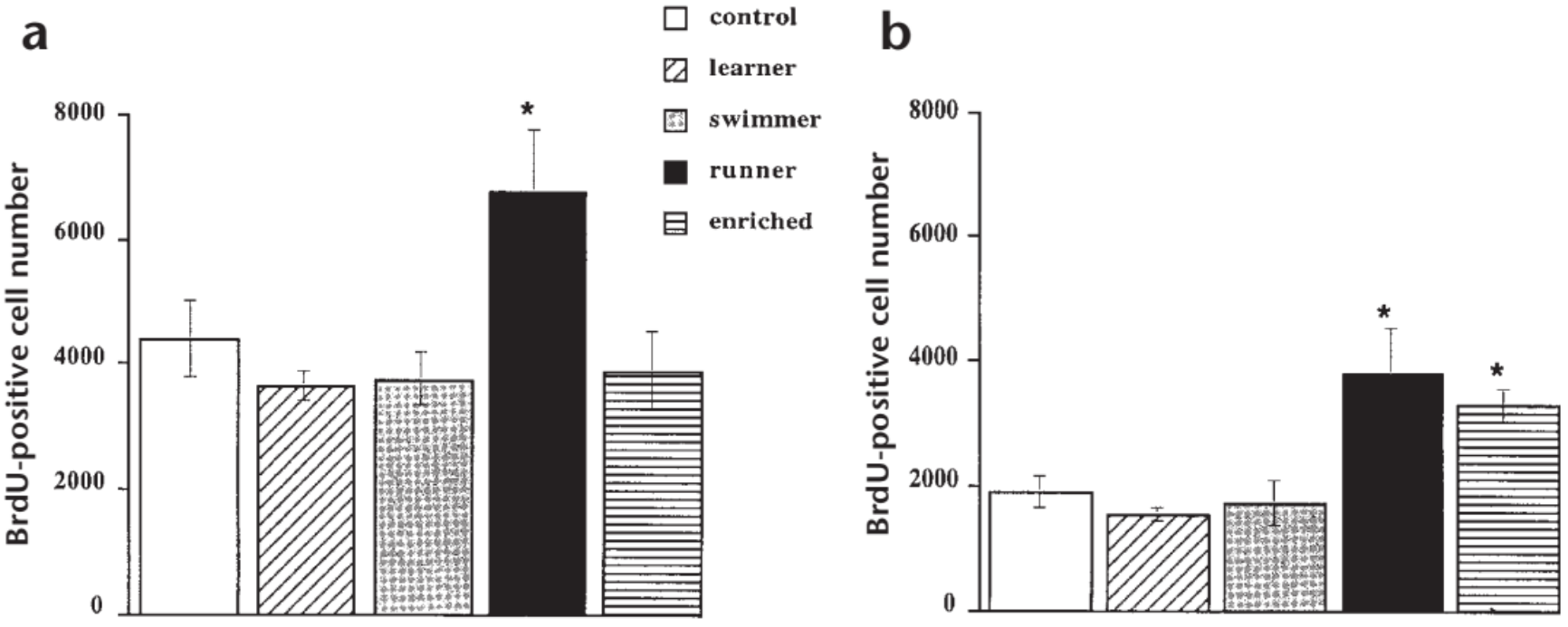
Correspondence should be addressed to F.H.G. (fgage@salk.edu)


a
b
c

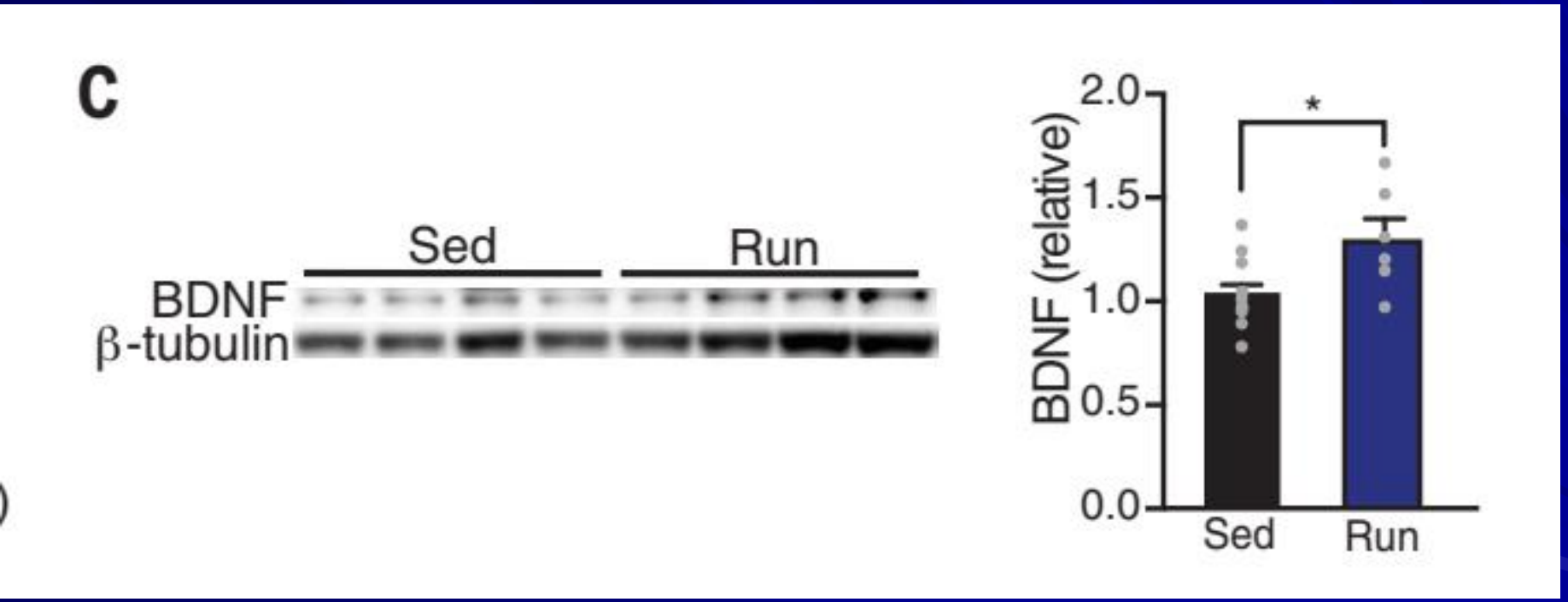

a
b
control
learner
swimmer
runner
enriched
BrdU-positive cell number
8000
6000
4000
2000
0
*

AGING

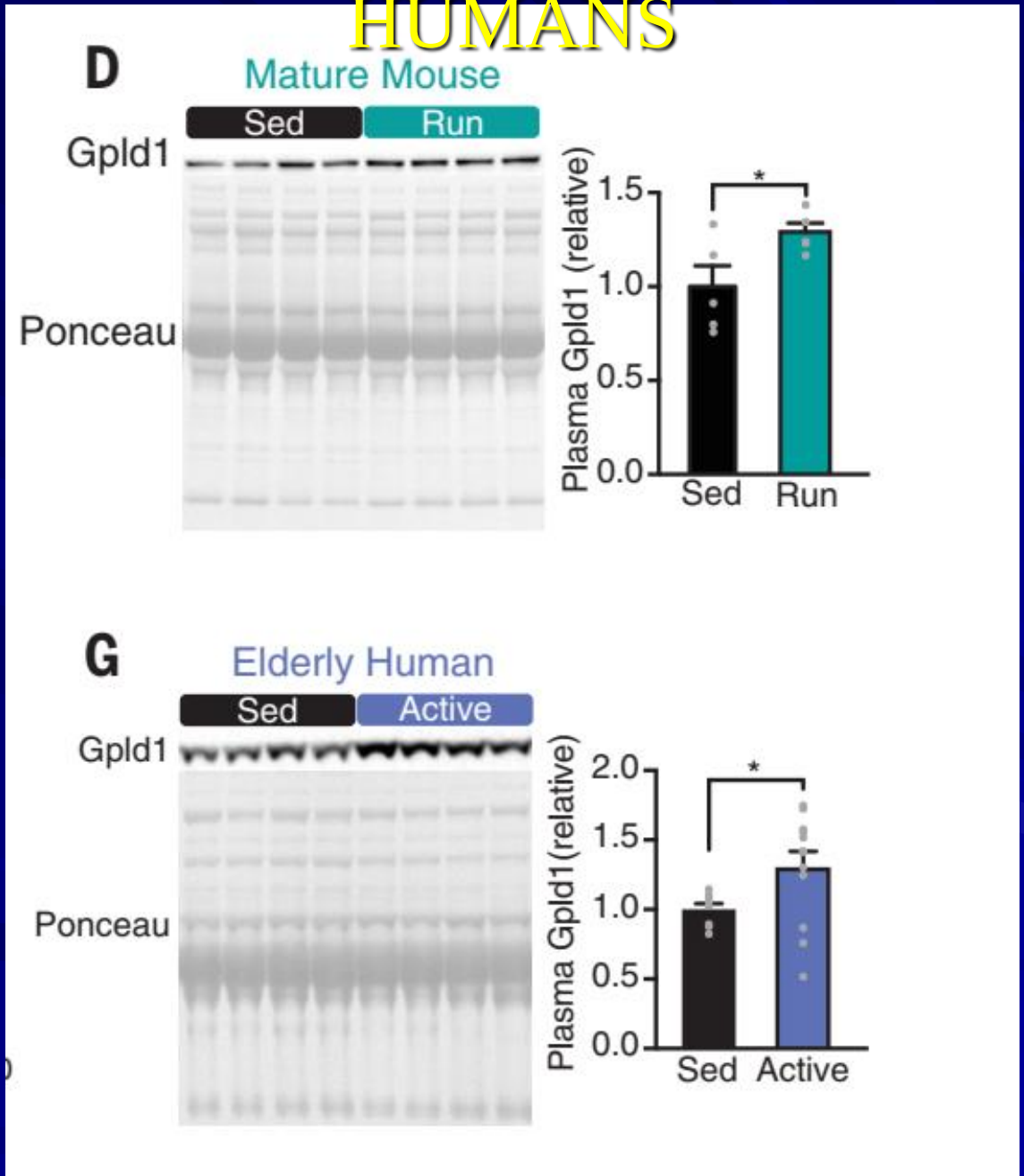
Blood factors transfer beneficial effects of exercise on neurogenesis and cognition to the aged brain

Alana M. Horowitz[1,2]*, Xuelai Fan[1]*, Gregor Bieri[1], Lucas K. Smith[1,2], Cesar I. Sanchez-Diaz[1], Adam B. Schroer[1], Geraldine Gontier[1], Kaitlin B. Casaletto[3,4], Joel H. Kramer[3,4], Katherine E. Williams[5], Saul A. Villeda[1,2,6,7]†

Horowitz *et al.*, *Science* **369**, 167–173 (2020) 10 July 2020


C
Sed
Run
BDNF
β-tubulin
BDNF (relative)
2.0
1.5
1.0
0.5
0.0
*
Sed
Run

INCREASES OF PHOSPPHOLIPASE D1 IN HUMANS



NEUROGENIC INTERVENTIONS

HHS Public Access

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Neurobiol Learn Mem. 2014 November ; 115: 3–9. doi:10.1016/j.nlm.2014.08.012.

Mental and Physical (MAP) Training: A Neurogenesis-Inspired Intervention that Enhances Health in Humans

Tracey J. Shors[1,2,4], **Ryan L. Olson**[3], **Marsha E. Bates**[2,5], **Edward A. Selby**[2], and **Brandon L. Alderman**[3]

[1]Behavioral and Systems Neuroscience, Rutgers University

[2]Department of Psychology, Rutgers University

[3]Department of Exercise Science, Rutgers University

[4]Center for Collaborative Neuroscience, Rutgers University

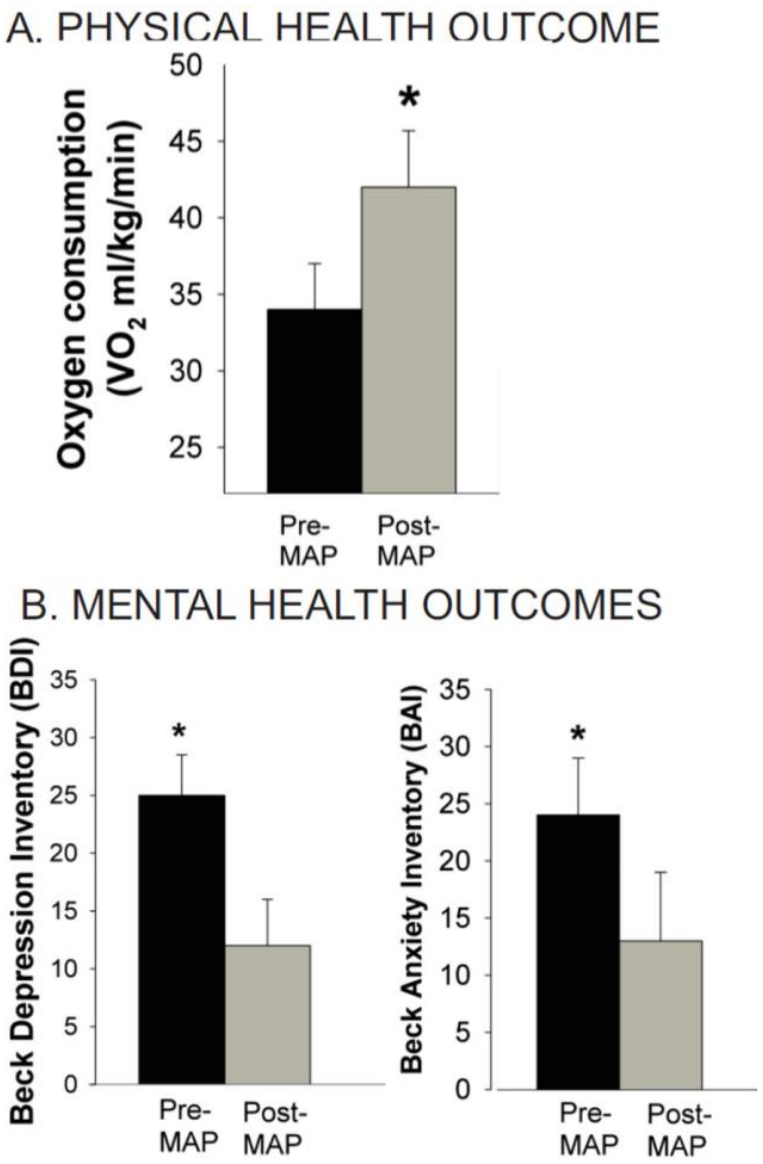
[5]Center for Alcohol Studies, Rutgers University

MENTAL AND PHYSICAL map TRAINING℠

Mental Training:
- 30-min focused attention meditation
  (20-min sitting; 10-min walking)

Physical Training:
- 30-min aerobic exercise with motor skill training

2 supervised sessions a week for 8 weeks



frontiers in Neuroscience

ORIGINAL RESEARCH
published: 23 April 2018
doi: 10.3389/fnins.2018.00211

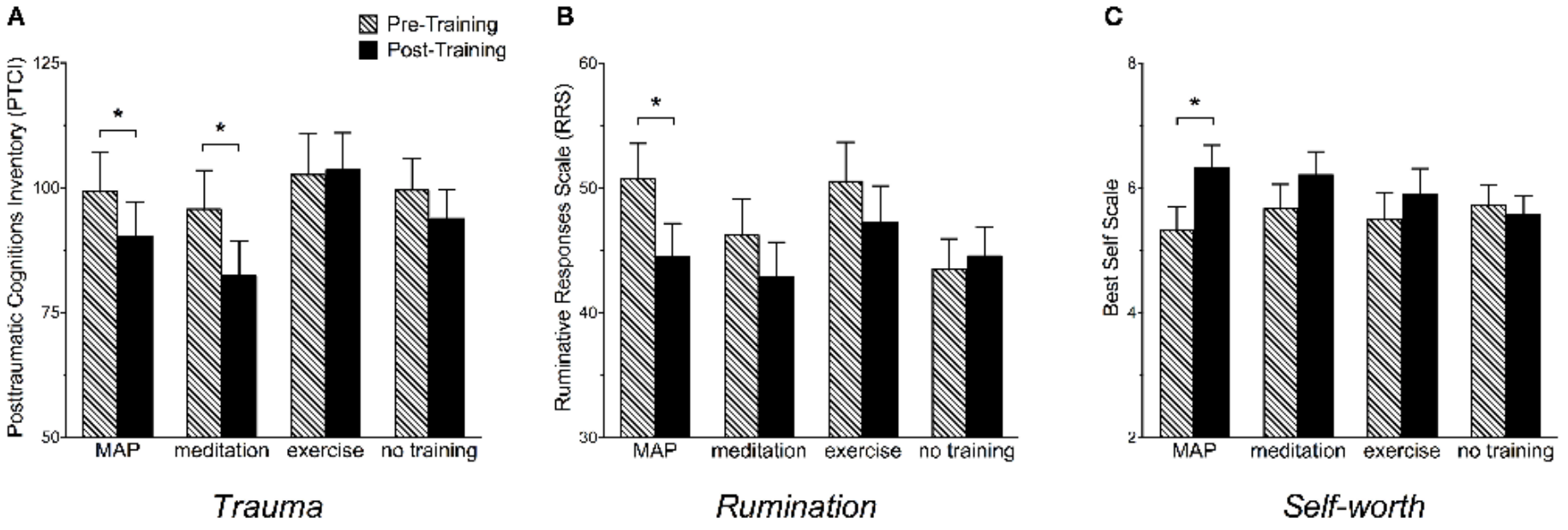
Check for updates

MAP Training My Brain™: Meditation Plus Aerobic Exercise Lessens Trauma of Sexual Violence More Than Either Activity Alone

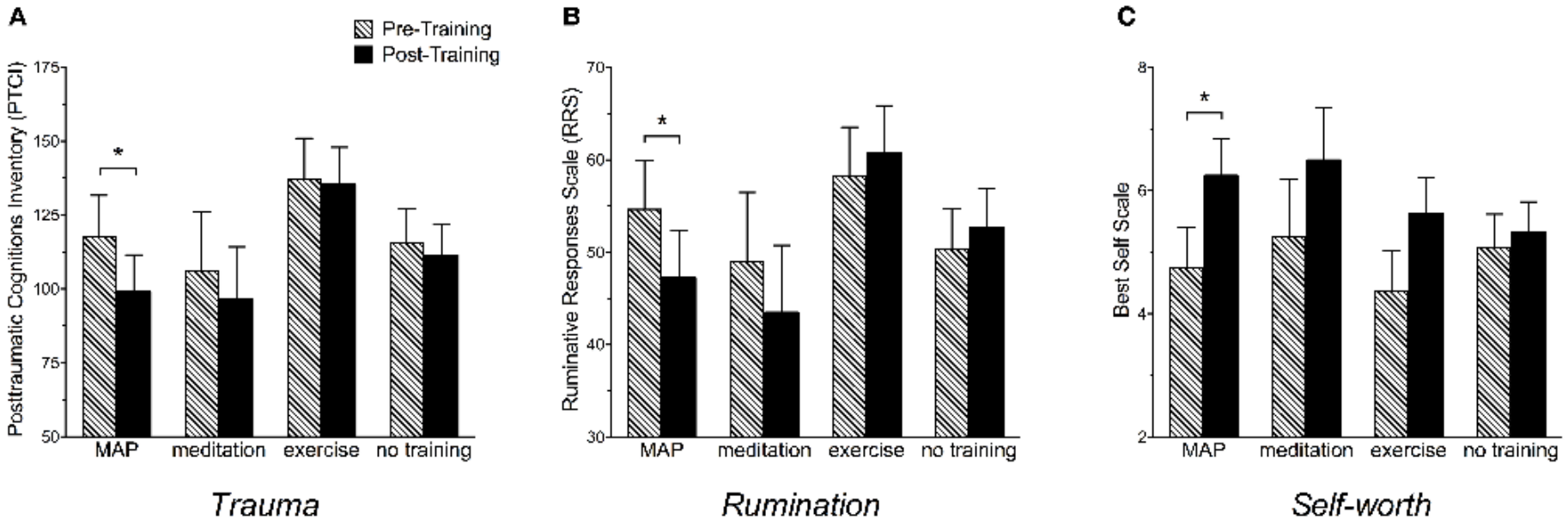
Tracey J. Shors, Han Y. M. Chang and Emma M. Millon*

Behavioral and Systems Neuroscience, Department of Psychology, Center for Collaborative Neuroscience, Rutgers University, Piscataway, NJ, United States

All women regardless of trauma or PTSD



Women with sexual violence history



OTHER NEUROGENIC INTERVENTIONS

Psychiatry Research: Neuroimaging 191 (2011) 36–43

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

Mindfulness practice leads to increases in regional brain gray matter density

Britta K. Hölzel[a,b,*], James Carmody[c], Mark Vangel[a], Christina Congleton[a], Sita M. Yerramsetti[a], Tim Gard[a,b], Sara W. Lazar[a]

[a] *Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
[b] *Bender Institute of Neuroimaging, Justus Liebig Universität Giessen, Germany*
[c] *University of Massachusetts Medical School, Worcester, MA, USA*

doi:10.1093/scan/nss076 SCAN (2013) 8, 34–39

Increased gray matter volume in the right angular and posterior parahippocampal gyri in loving-kindness meditators

Mei-Kei Leung,[1,2] Chetwyn C. H. Chan,[3,4] Jing Yin,[4,5] Chack-Fan Lee,[4,5] Kwok-Fai So,[4,6,7] and Tatia M. C. Lee[1,2,4,7,8]

[1]Laboratory of Neuropsychology, The University of Hong Kong, 852 Hong Kong, China, [2]Laboratory of Cognitive Affective Neuroscience, The University of Hong Kong, 852 Hong Kong, China, [3]Applied Cognitive Neuroscience Laboratory, Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, 852 Hong Kong, China, [4]Social Neuroscience Research Network, The University of Hong Kong, 852 Hong Kong, China, [5]Centre of Buddhist Studies, The University of Hong Kong, 852 Hong Kong, China, [6]Department of Anatomy, The University of Hong Kong, 852 Hong Kong, China, [7]The State Key Laboratory of Brain and Cognitive Sciences, The University of Hong Kong, 852 Hong Kong, China, and [8]Institute of Clinical Neuropsychology, The University of Hong Kong, 852 Hong Kong, China

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PLoS one

Interactivity and Reward-Related Neural Activation during a Serious Videogame

Steven W. Cole[1], Daniel J. Yoo[2], Brian Knutson[2]*

1 HopeLab Foundation, Redwood City, California, United States of America, **2** Department of Psychology, Stanford University, Stanford, California, United States of America

Genes Nutr (2009) 4:271–282
DOI 10.1007/s12263-009-0134-5

REVIEW

Impact of diet on adult hippocampal neurogenesis

Doris Stangl · Sandrine Thuret

Molecular Psychiatry (2014), 1–9
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www.nature.com/mp

ORIGINAL ARTICLE

The P7C3 class of neuroprotective compounds exerts antidepressant efficacy in mice by increasing hippocampal neurogenesis

AK Walker[1,2], PD Rivera[2], Q Wang[1,2], J-C Chuang[1,2], S Tran[3], S Osborne-Lawrence[1,2], SJ Estill[3], R Starwalt[3], P Huntington[3], L Morlock[3], J Naidoo[3], NS Williams[3], JM Ready[3], AJ Eisch[2], AA Pieper[4,5] and JM Zigman[1,2,5]

THE UTINGA PROTOCOLO

Handbook of Clinical Neurology, Vol. 158 (3rd series)
Sports Neurology
B. Hainline and R.A. Stern, Editors
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Chapter 1

Sports and the human brain: an evolutionary perspective

IAN J. WALLACE[1]*, CLOTILDE HAINLINE[2], AND DANIEL E. LIEBERMAN[1]
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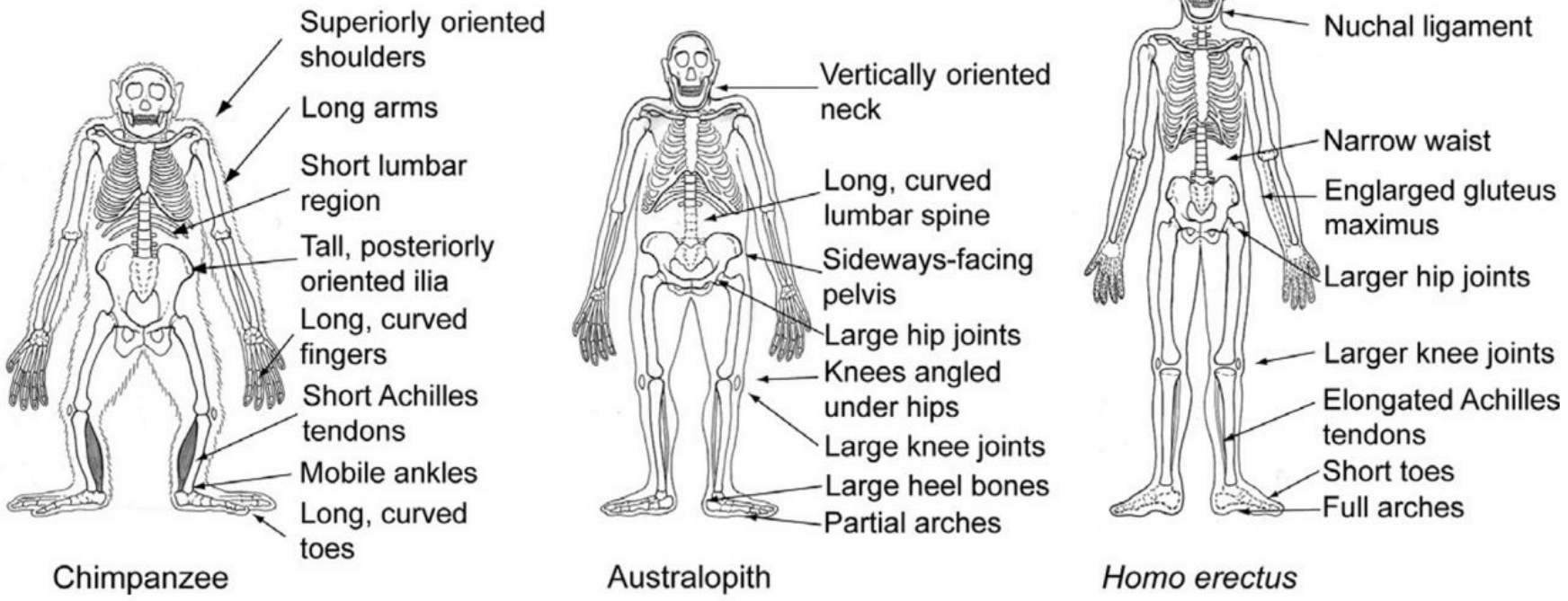
[2]*Department of Neurology, Boston University School of Medicine, Boston, MA, United States*


Superiorly oriented shoulders
Long arms
Short lumbar region
Tall, posteriorly oriented ilia
Long, curved fingers
Short Achilles tendons
Mobile ankles
Long, curved toes
Chimpanzee
Vertically oriented neck
Long, curved lumbar spine
Sideways-facing pelvis
Large hip joints
Knees angled under hips
Large knee joints
Large heel bones
Partial arches
Australopith
Nuchal ligament
Narrow waist
Englarged gluteus maximus
Larger hip joints
Larger knee joints
Elongated Achilles tendons
Short toes
Full arches
Homo erectus

CONCLUSION
THE SECRET OF THE SEAHORSE