

NEUROPEDIATRÍA

Revisión tópicos de interés en Neurodesarrollo para el Pediatra

Sociedad Chilena de Pediatría Filial Los Lagos

DR. PATRICIO GUERRA



DIAGNÓSTICOS PEDIÁTRICOS

-PATOLOGÍA O MORBILIDAD INTERCORRENTE

-ESTADO NUTRICIONAL

-DESARROLLO PSICOMOTOR

LA

MORTALIDAD de los NIÑOS EN CHILE

Por los Doctores L. Sierra M. y Eduardo Moore

ESTUDIO ENVIADO POR EL SEÑOR
AUGUSTO MATTE, MINISTRO DE CHILE EN FRANCIA, A LA OFICINA
DE LA 1.^a CIRCUNSCRIPCION DEL REGISTRO CIVIL
EN VALPARAISO.

Publicacion de la Sociedad Protectora de la Infancia.

VALPARAISO:
IMPRENTA Y LITOGRAFIA CENTRAL

1896.

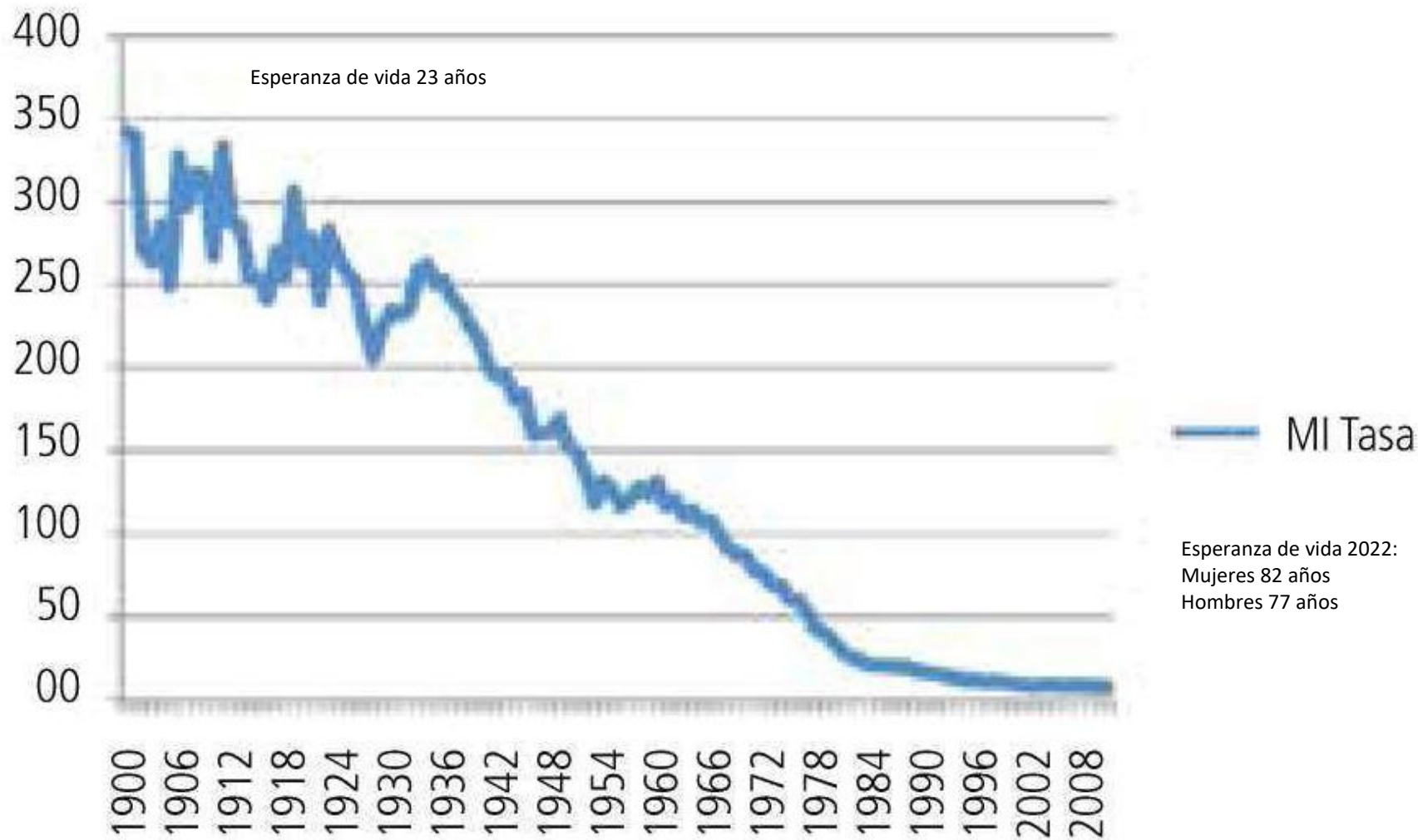


CHILE tiene la más alta mortalidad infantil del Mundo.

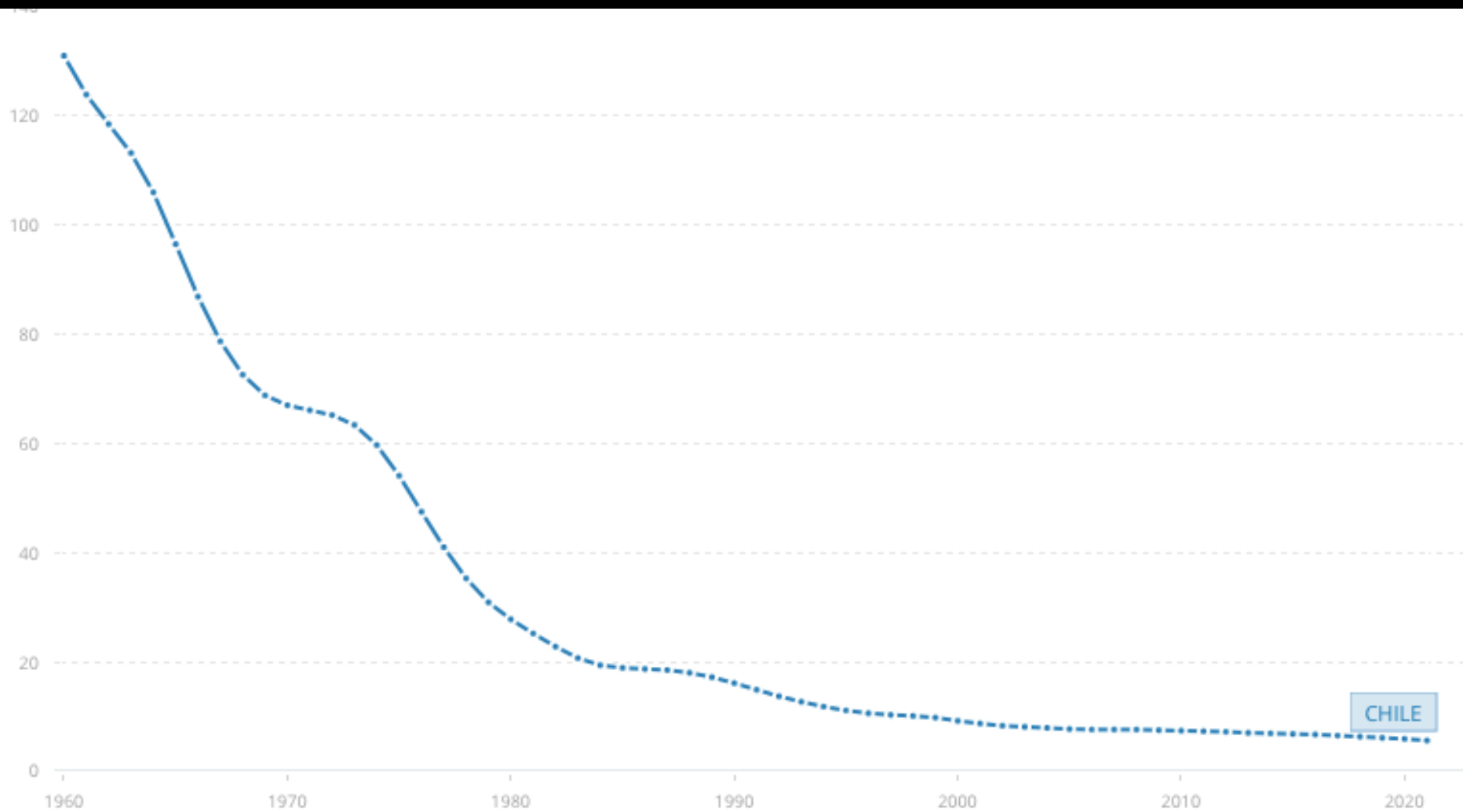
Por cada veinte partos, nace un niño muerto. La mortalidad nuestra equivale al 50,5% de los nacidos vivos; por cada mil nacidos vivos mueren doscientos cincuenta. Por cada diez niños nacidos vivos muere uno antes del primer mes de vida; la cuarta parte, antes del primer año; y casi la mitad antes de cumplir nueve años. Cuatrocientos mil niños no concurren anualmente a ninguna Escuela, lo que representa el 42% de la población en edad escolar. Tenemos seiscientos mil jóvenes analfabetos. El 27,9% de los nacidos vivos son hijos ilegítimos. cifra ésta la más alta entre los países civilizados.

Tasa de Mortalidad Infantil 1900-2008

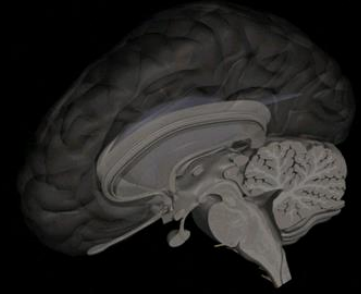
(Recién nacidos vivos que mueren antes del año de vida)



Tasa de Mortalidad Infantil 1960-2024
(Recién nacidos vivos que mueren antes del año de vida)
2024: 6,2/1.000 RN vivos



Fuente: www.datos.bancomundial.org



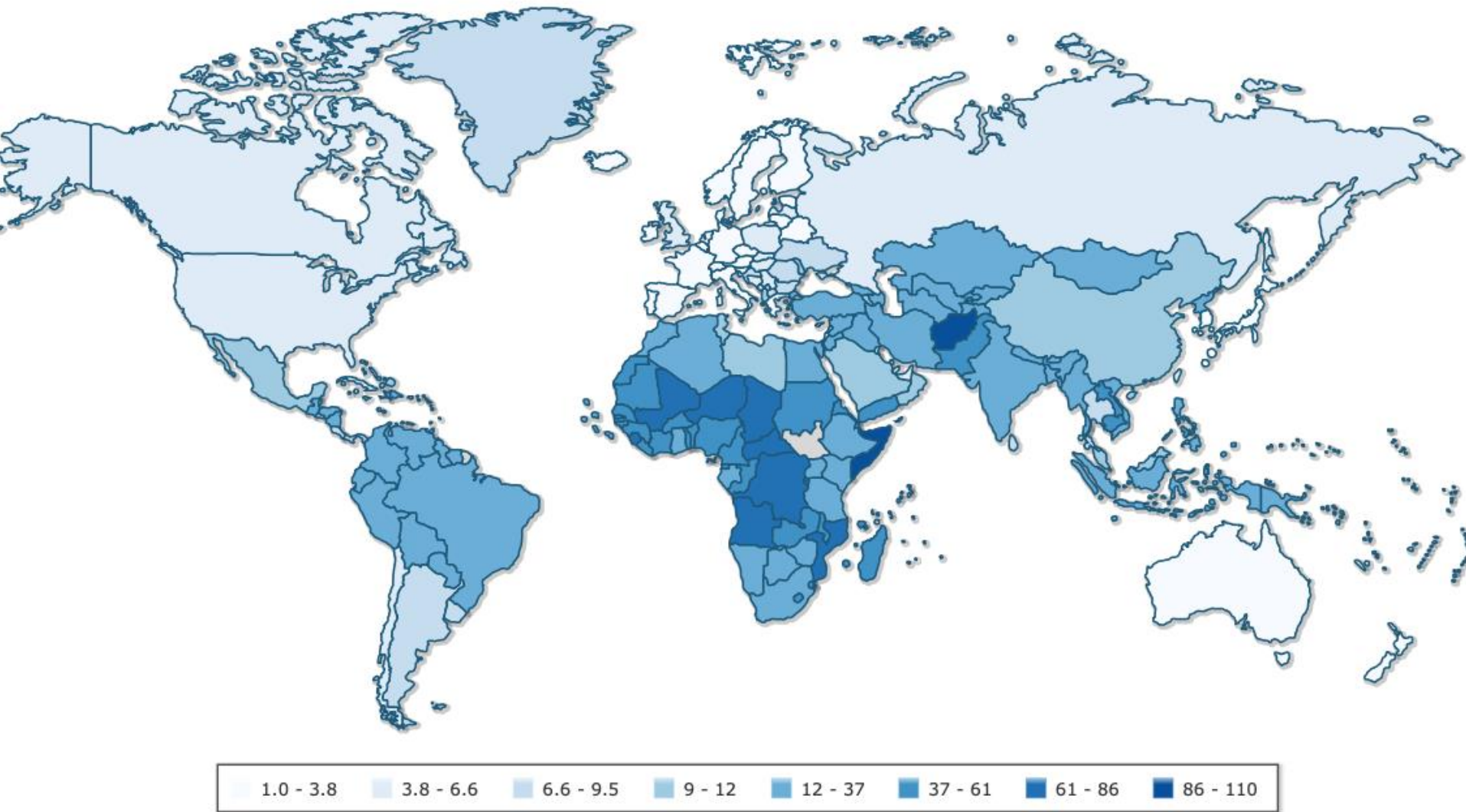
DIAGNÓSTICOS PEDIÁTRICOS

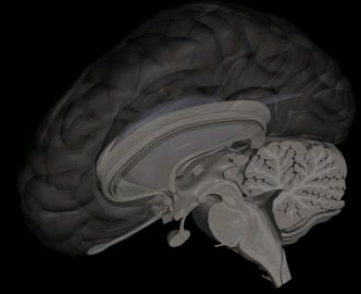
-PATOLOGÍA O MORBILIDAD INTERCURRENTE

-ESTADO NUTRICIONAL

-DESARROLLO PSICOMOTOR

Mapa mundial de Mortalidad Infantil





DIAGNÓSTICOS PEDIÁTRICOS

-PATOLOGÍA O MORBILIDAD INTERCURRENTE

-ESTADO NUTRICIONAL

-DESARROLLO PSICOMOTOR

DISMINUCIÓN NACIMIENTOS

DISMINUCIÓN MORTALIDAD INFANTIL

AUMENTO DE SECUELAS DE NIÑOS QUE YA NO MUEREN (PREMATUROS)

AUMENTO DE CONDICIONES DE SALUD CRÓNICAS (CARDIOPATÍAS, NEUROLOGÍA)

AUMENTO DE CONDICIONES ANTERIORMENTE NO RECONOCIDAS (AUTISMO)

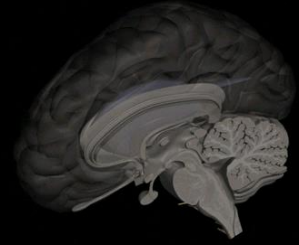
AUMENTO DE CONDICIONES NUEVAS Y CONDICIONADAS SOCIALMENTE (TDAH)

SENSACIÓN DE MAYOR CARGA DE ENFERMEDAD EN LA INFANCIA

¿QUÉ PODEMOS HACER PARA DISMINUIR ESTA SENSACIÓN? (O ESTA REALIDAD)



GOODWIN (DINAMARCA) 1974



110 NIÑOS DADOS EN ADOPCIÓN

55 VARONES HIJOS DE PADRES ALCOHÓLICOS

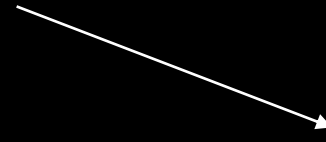
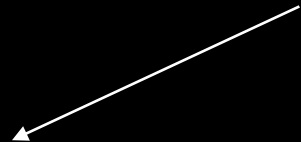
55 VARONES PADRES NO ALCOHÓLICOS



ADOPCIÓN ANTES DEL MES DE VIDA-NUNCA CONTACTO CON PADRES.

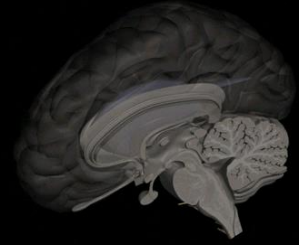


25-29 AÑOS DE EDAD

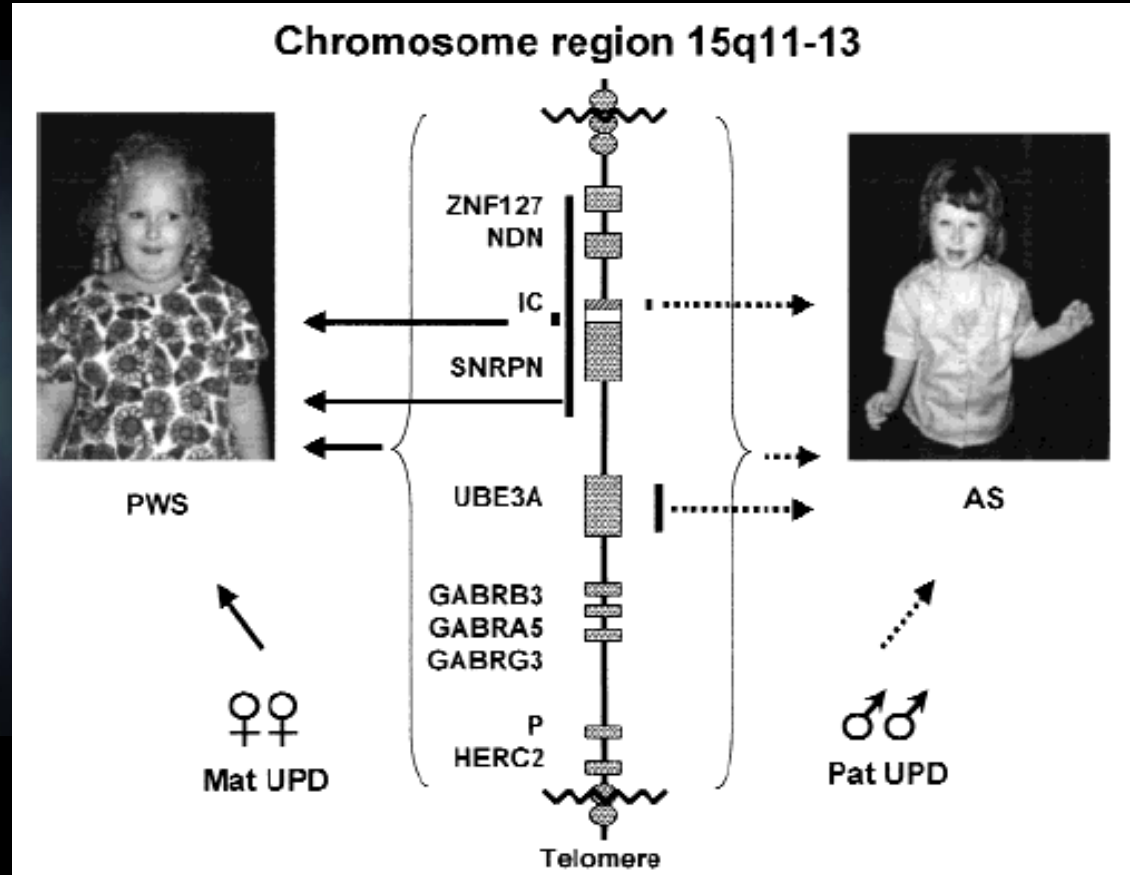
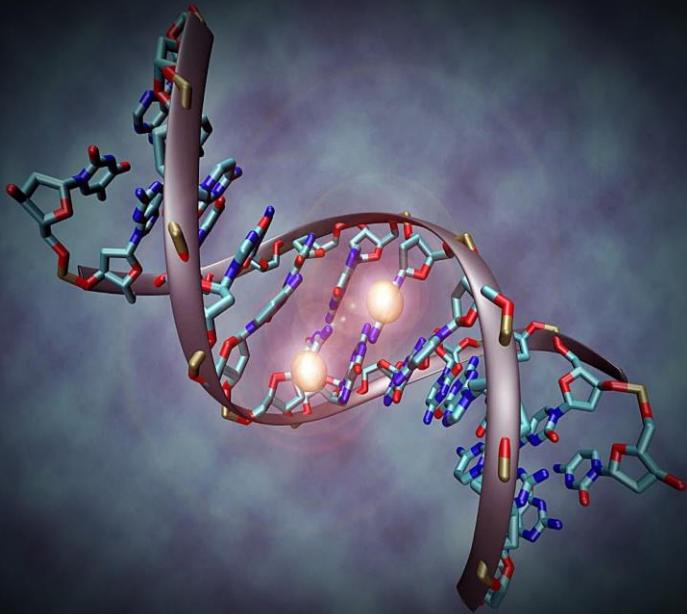


20% ALCOHOLISMO

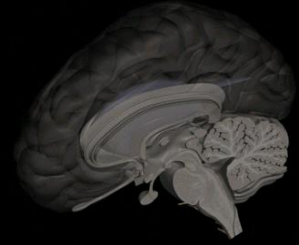
5% ALCOHOLISMO



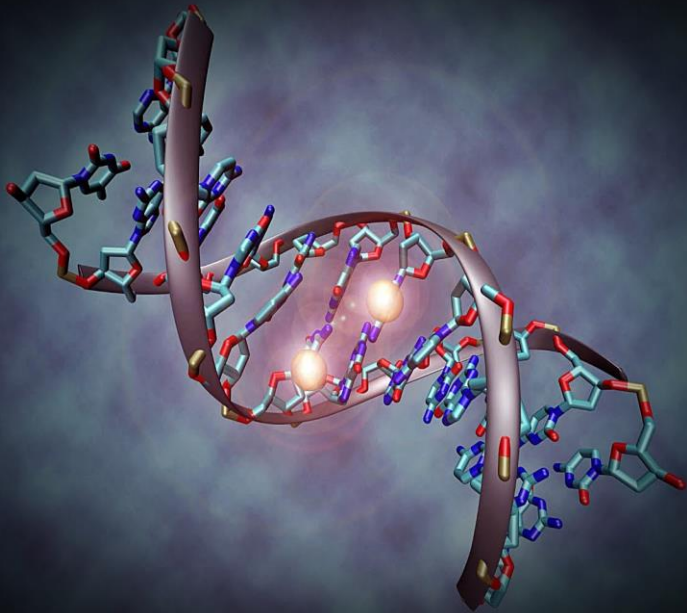
MECANISMOS DE CAMBIO: MUTACIONES

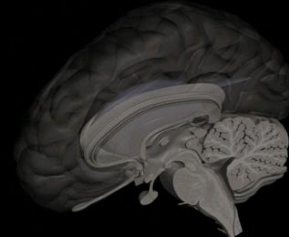


100 variantes de novo (mutaciones) identificables en relación a nuestros padres



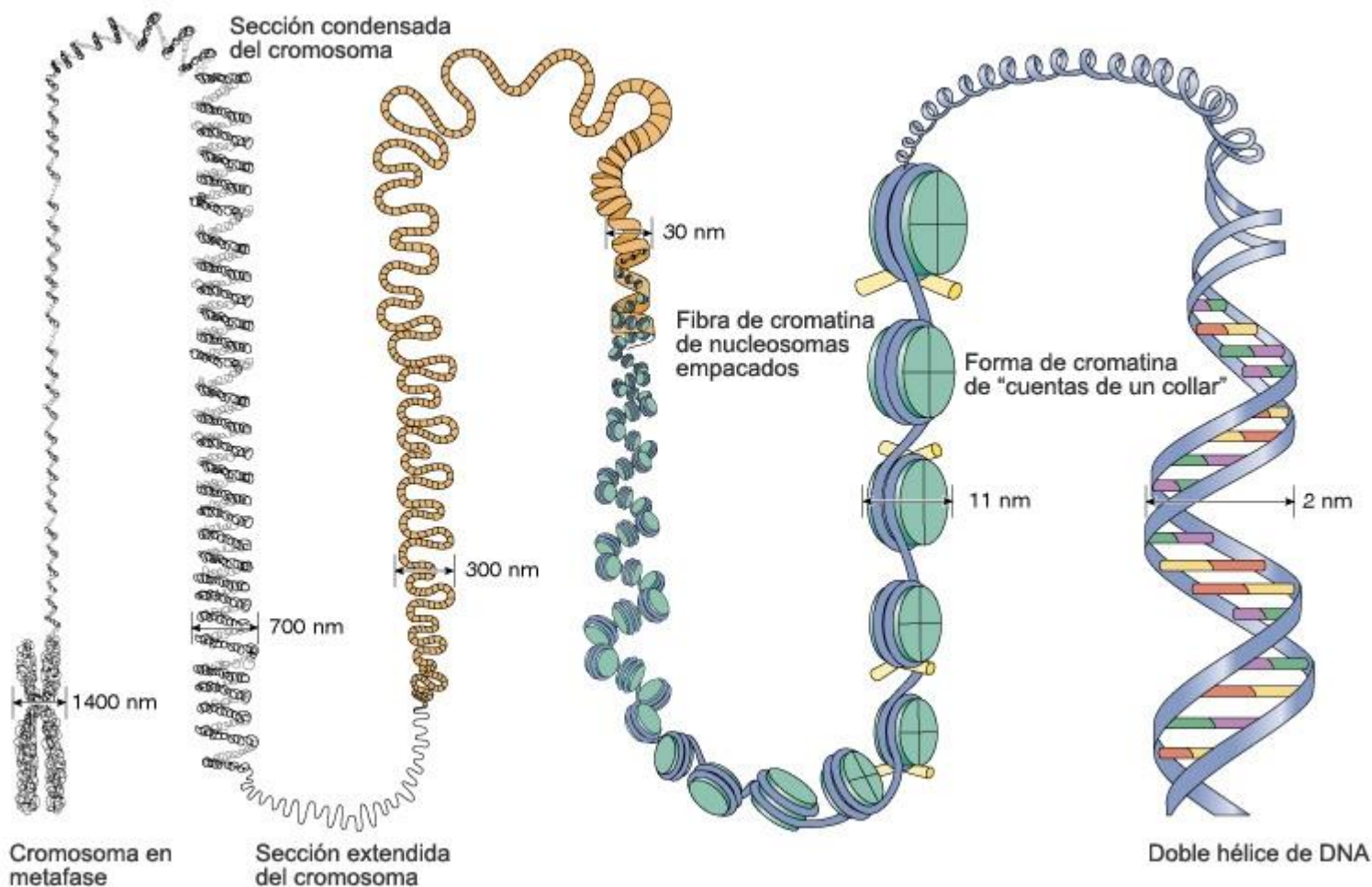
MECANISMOS DE CAMBIO: INFLUENCIA AMBIENTAL





Se entiende por epigenética al “estudio de cambios heredables en la función de los genes que ocurren sin un cambio en la secuencia del ADN”.

MECANISMOS DE CAMBIO: EPIGENÉTICA



Published in final edited form as:

Horm Behav. 2011 March ; 59(3): 315–320. doi:10.1016/j.yhbeh.2010.05.005.

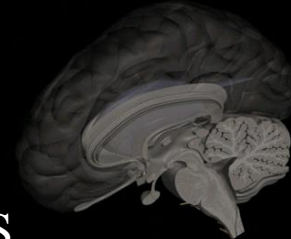
Epigenetic marking of the BDNF gene by early-life adverse experiences

Tania L. Roth^{1,2} and J. David Sweatt^{1,*}

¹ Department of Neurobiology and Evelyn F. McKnight Brain Institute, University of Alabama at Birmingham, Birmingham, AL 35294

Abstract

Studies over the past half-century have made it clear that environmental influences in development, particularly stress and traumatic experiences, can remain pervasive across the lifespan. Though it has been hypothesized for some time that the long-term consequences of early-life adversity represent epigenetic influences, it has not been until recently that studies have begun to provide empirical support of experience-driven epigenetic modifications to the genome. Here we focus on this theme, and review current knowledge pertaining to the epigenetics of behavioral development. At the center of our discussion is the brain-derived neurotrophic factor (BDNF) gene, as abnormal BDNF gene activity is a leading etiological hypothesis by which early-life adverse experiences persistently modify brain and behavioral plasticity.



**EXPERIENCIAS ADVERSAS
EN LA INFANCIA**



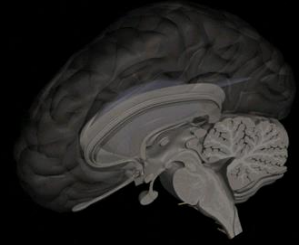
**MODIFICACIÓN EXPRESIÓN
DEL GEN BDNF**



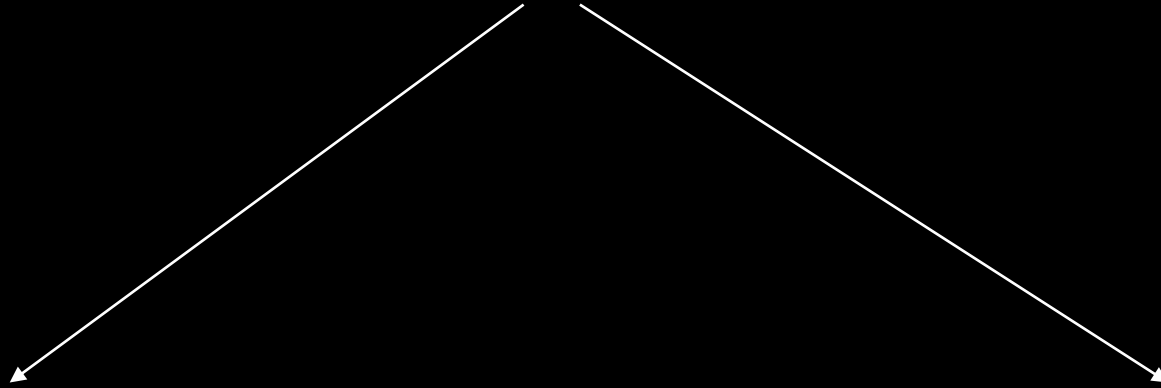
**RESPUESTA ANSIOGÉNICA EXAGERADA
FRENTE A ESTRÉS**



**EVIDENCIA MANTENCIÓN DE LA MODIFICACIÓN DE LA EXPRESIÓN
DEL GEN BDNF AL MENOS HASTA LA TERCERA GENERACIÓN**



TEMPERAMENTO



FÁCIL

MATRIZ BIOLÓGICA

DIFÍCIL

TEMPERAMENTO

+

AMBIENTE=

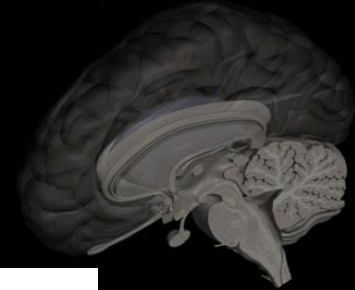
CARÁCTER

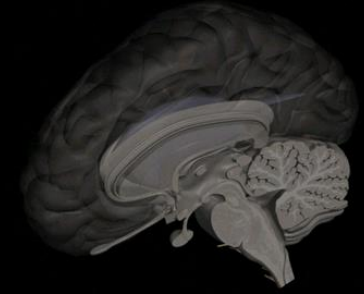
COGNITIVE AND ATTENTIONAL MECHANISMS IN DELAY OF GRATIFICATION¹

WALTER MISCHEL,² EBBE B. EBBESEN, AND ANTONETTE RASKOFF ZEISS

Stanford University

Three experiments investigated attentional and cognitive mechanisms in delay of gratification. In each study preschool children could obtain a less preferred reward immediately or continue waiting indefinitely for a more preferred but delayed reward. Experiment I compared the effects of external and cognitive distraction from the reward objects on the length of time which preschool children waited for the preferred delayed reward before forfeiting it for the sake of the less preferred immediate one. In accord with predictions from an extension of frustrative nonreward theory, children waited much longer for a preferred reward when they were distracted from the rewards than when they attended to them directly. Experiment II demonstrated that only certain cognitive events (thinking "fun things") served as effective ideational distractors. Thinking "sad thoughts" produced short delay times, as did thinking about the rewards themselves. In Experiment III the delayed rewards were not physically available for direct attention during the delay period, and the children's attention to them cognitively was manipulated by prior instructions. While the children waited, cognitions about the rewards significantly reduced, rather than enhanced, the length of their delay of gratification. Overall, attentional and cognitive mechanisms which enhanced the salience of the rewards shortened the length of voluntary delay, while distractions from the rewards, overtly or cognitively, facilitated delay. The results permit a reinterpretation of basic mechanisms in voluntary delay of gratification and self-control.





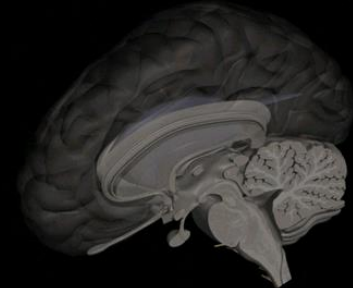
EXPERIENCIA DE AUTOCONTROL PREESCOLARES EVOLUCIÓN A 30 AÑOS

-70% “SE AGUANTABAN”

-30% “NO SE AGUANTARON”

DIFERENCIAS SIGNIFICATIVAS EN EVOLUCIÓN

- SOCIAL
- ESCOLAR
- EMOCIONAL
- FAMILIAR
- LABORAL



Behavioral and neural correlates of delay of gratification 40 years later

B. J. Casey^{a,1}, Leah H. Somerville^a, Ian H. Gotlib^b, Ozlem Ayduk^c, Nicholas T. Franklin^a, Mary K. Askren^d, John Jonides^d, Marc G. Berman^d, Nicole L. Wilson^e, Theresa Teslovich^a, Gary Glover^f, Vivian Zayas^g, Walter Mischel^{h,1}, and Yuichi Shoda^{e,1}

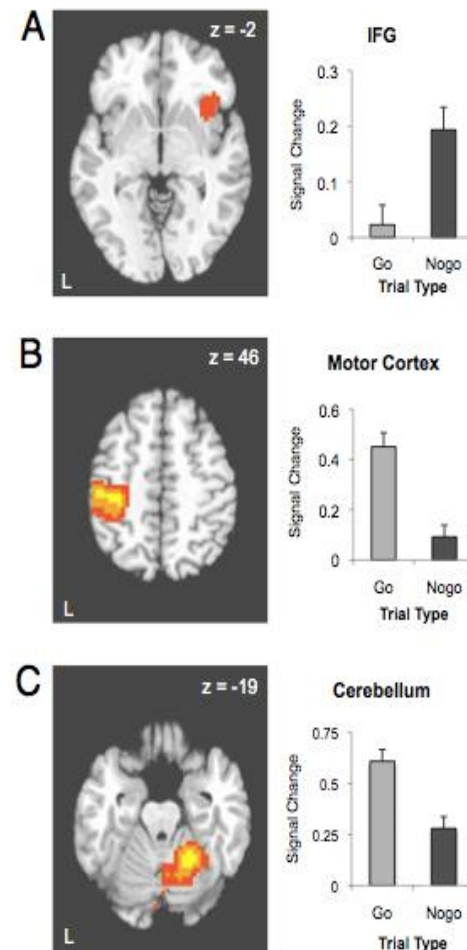
^aSackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY 10065; ^bDepartment of Psychology, Stanford University, Stanford, CA 94305; ^cDepartment of Psychology, University of California, Berkeley, CA 94720; ^dDepartment of Psychology, University of Michigan, Ann Arbor, MI 48109; ^eDepartment of Psychology, University of Washington, Seattle, WA 98195; ^fLucas Imaging Center, Department of Radiology, Stanford University School of Medicine, Stanford, CA 94305; ^gDepartment of Psychology, Cornell University, Ithaca, NY 14853; and ^hDepartment of Psychology, Columbia University, New York, NY 10027

Edited* by Michael Posner, University of Oregon, Eugene, OR, and approved July 26, 2011 (received for review May 27, 2011)

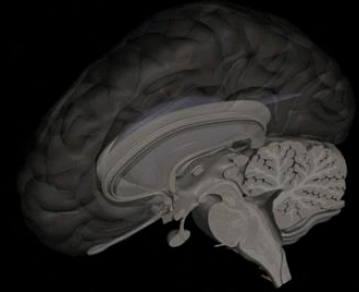
We examined the neural basis of self-regulation in individuals from a cohort of preschoolers who performed the delay-of-gratification task 4 decades ago. Nearly 60 individuals, now in their mid-forties, were tested on “hot” and “cool” versions of a go/nogo task to assess whether delay of gratification in childhood predicts impulse control abilities and sensitivity to alluring cues (happy faces). Individuals who were less able to delay gratification in preschool and consistently showed low self-control abilities in their twenties and thirties performed more poorly than did high delayers when having to suppress a response to a happy face but not to a neutral or fearful face. This finding suggests that sensitivity to environmental hot cues plays a significant role in individuals’ ability to suppress actions toward such stimuli. A subset of these participants ($n = 26$) underwent functional imaging for the first time to test for biased recruitment of frontostriatal circuitry when required to suppress responses to alluring cues. Whereas the prefrontal cortex differentiated between nogo and go trials to a greater extent in high delayers, the ventral striatum showed exaggerated recruitment in low delayers. Thus, resistance to temptation as measured originally by the delay-of-gratification task is a relatively stable individual difference that predicts reliable biases in frontostriatal circuitries that integrate motivational and control processes.

had more difficulty suppressing inappropriate actions than did their low-temptation-focus counterparts, especially for the most difficult trials. Difficulty was manipulated by increasing the number of “go” trials preceding a “nogo” trial, thus making the “go” response more salient and automated. Differences between the high- and low-temptation-focus groups increased as the number of preceding “go” trials increased, with the high-temptation-focus group having more difficulty, reflected in slower response times, suppressing responses. These findings suggest that performance in preschool delay of gratification may predict the capacity, in adulthood, to control thoughts and actions, as reflected in performance on cognitive control tasks, and that the ability to control one’s thoughts and actions can vary by the potency of interfering information (12). Likewise, alluring or social contexts can diminish self-control (4, 13, 14).

Early experiments on delay of gratification demonstrated that part of the contextual effect was due to the different cognitive strategies that individuals used. For example, “cooling” the hot, appealing, or appetitive features of tempting stimuli by reappraisal or reframing strategies to focus on their cool, cognitive features (e.g., to envision the marshmallow as a cloud or a little cotton ball, rather than as a sweet, delectable treat) has been shown to be highly effective in enhancing delay of gratification



EXPERIENCIA DE AUTOCONTROL PREESCOLARES EVOLUCIÓN A 30 AÑOS



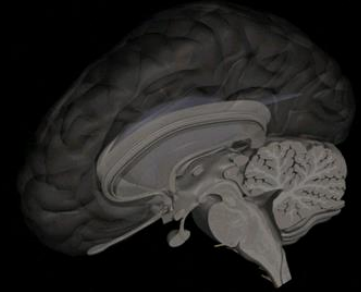
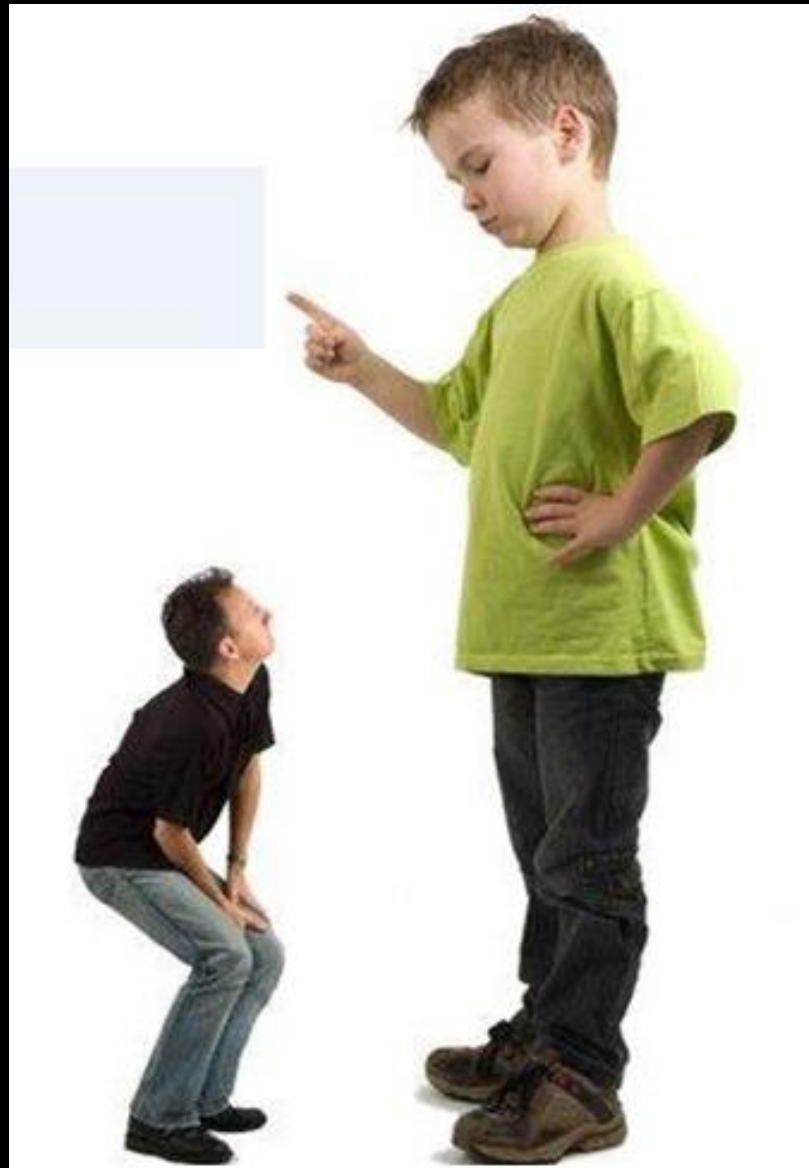
AUTOCONTROL → CAPACIDAD DE SUPERAR LA
GRATIFICACIÓN INMEDIATA
EN POS DE ALGO “SUPERIOR”

NIÑOS CON CAPACIDAD INNATA

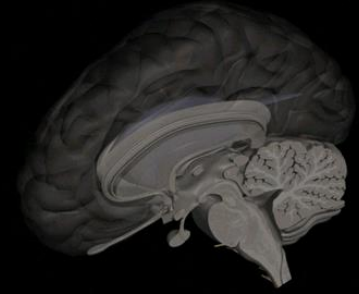
NIÑOS QUE SE LES PUEDE “ENTRENAR”

PRIMER PASO → CONTROL EXTERNO

LUEGO → DESARROLLO DE CONTROL INTERNO



POR LO TANTO, EN BASE AL CONOCIMIENTO ACTUAL:



-EN LOS PATRONES CONDUCTUALES NEUROBIOLÓGICOS HAY UNA MEZCLA DE FACTORES BIOLÓGICOS Y AMBIENTALES

-EN LA MAYORÍA DE LOS TRASTORNOS DEL NEURODESARROLLO (TEA-TDAH) SI BIEN PREDOMINA LA CARGA BIOLÓGICA, LAS INTERVENCIONES AMBIENTALES TEMPRANAS, PUEDEN MODULAR ESTA CARGA BIOLÓGICA

¿QUÉ INTERVENCIONES AMBIENTALES TEMPRANAS PUEDE RECOMENDAR EL PEDIATRA PARA ASÍ EVITAR QUE SEA NECESARIO DERIVAR A UN NEURÓLOGO, AÑOS DESPUÉS, A UN NIÑO?

Maternal-Preterm Skin-to-Skin Contact Enhances Child Physiologic Organization and Cognitive Control Across the First 10 Years of Life

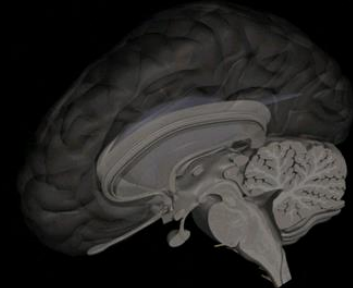
Ruth Feldman, Zehava Rosenthal, and Arthur I. Eidelman

Background: Maternal–newborn contact enhances organization of the infant’s physiological systems, including stress reactivity, autonomic functioning, and sleep patterns, and supports maturation of the prefrontal cortex and its ensuing effects on cognitive and behavioral control. Premature birth disrupts brain development and is associated with maternal separation and disturbances of contact-sensitive systems. However, it is unknown whether the provision of maternal–preterm contact can improve long-term functioning of these systems.

Methods: We used the Kangaroo Care (KC) intervention and provided maternal–newborn skin-to-skin contact to 73 premature infants for 14 consecutive days compared with 73 case-matched control subjects receiving standard incubator care. Children were then followed seven times across the first decade of life and multiple physiologic, cognitive, parental mental health, and mother–child relational measures were assessed.

Results: KC increased autonomic functioning (respiratory sinus arrhythmia, RSA) and maternal attachment behavior in the postpartum period, reduced maternal anxiety, and enhanced child cognitive development and executive functions from 6 months to 10 years. By 10 years of age, children receiving KC showed attenuated stress response, improved RSA, organized sleep, and better cognitive control. RSA and maternal behavior were dynamically interrelated over time, leading to improved physiology, executive functions, and mother–child reciprocity at 10 years.

Conclusions: These findings are the first to demonstrate long-term effects of early touch-based intervention on children’s physiologic organization and behavioral control and have salient implications for the care practices of premature infants. Results demonstrate the dynamic cascades of child physiological regulation and parental provisions in shaping developmental outcome and may inform the construction of more targeted early interventions.



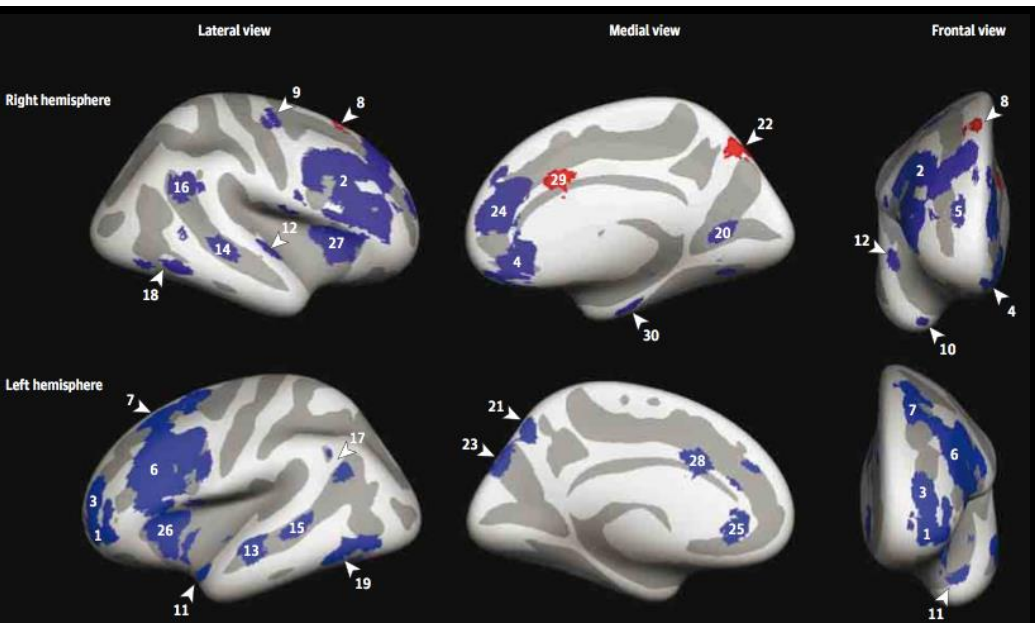
Original Investigation

Effect of Early Adversity and Childhood Internalizing Symptoms on Brain Structure in Young Men

Sarah K. G. Jensen, MSc; Erin W. Dickie, PhD; Deborah H. Schwartz, MA; C. John Evans, PhD; Iroise Dumontheil, PhD; Tomáš Paus, MD, PhD; Edward D. Barker, PhD

JAMA Pediatr. doi:10.1001/jamapediatrics.2015.1486

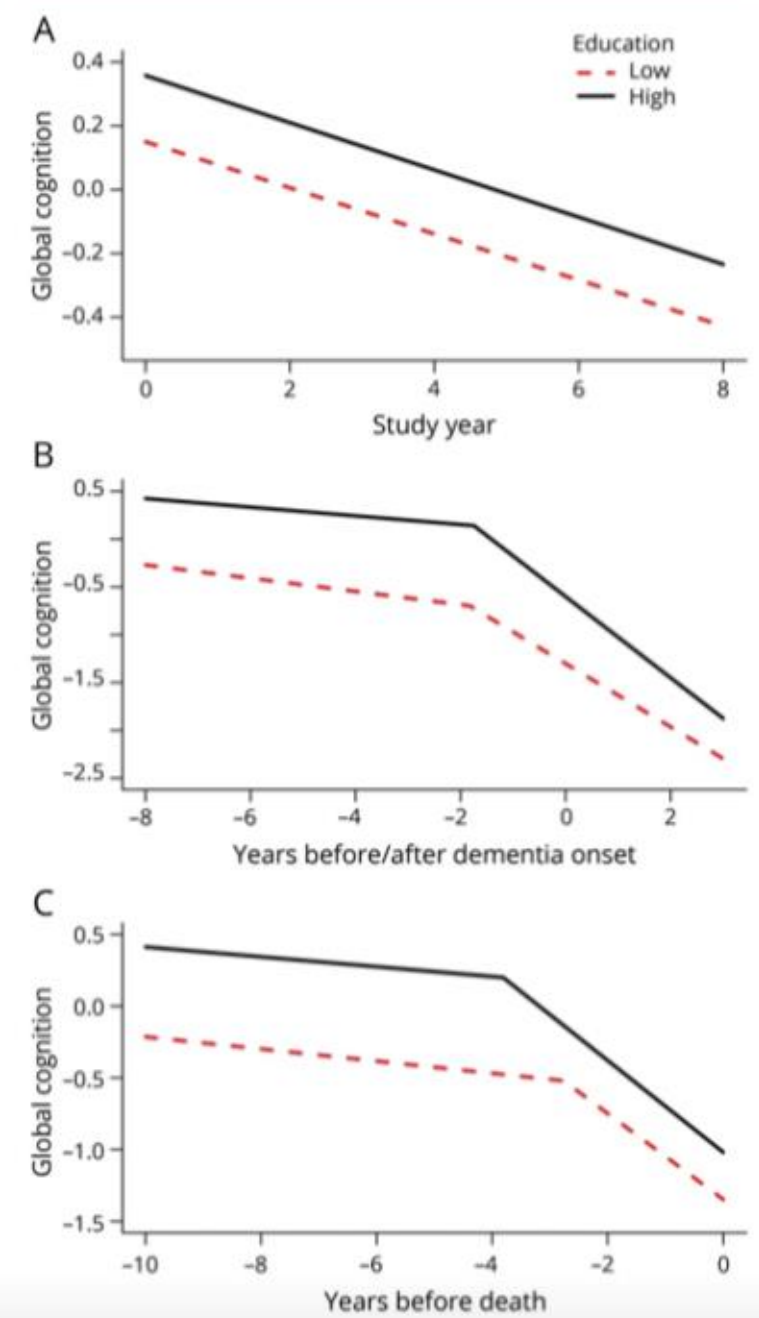
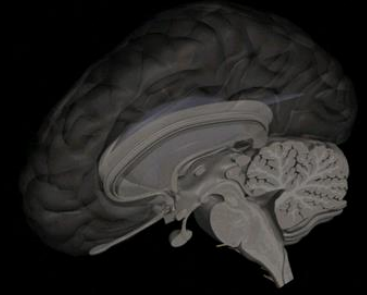
Published online August 17, 2015.



At a Glance

- The extent to which brain structure variation typically associated with depression may also relate to early experiences of stress was examined within a large (n = 494) longitudinal birth cohort.
- The study found that early adverse experiences predicted lower gray matter volume in the anterior cingulate cortex and greater gray matter volume in the precuneus in adolescence.
- Early adversity was indirectly associated with lower gray matter volume in the superior frontal gyrus via higher levels of internalizing symptoms.
- These results indicate that early childhood adversity is associated with altered brain structure, and the effects of depression on the brain may partly relate to early adversity.

Figure 1 Relation of education to trajectories of global cognitive change



Education and cognitive reserve in old age

Robert S. Wilson, PhD, Lei Yu, PhD, Melissa Lamar, PhD, Julie A. Schneider, MD, Patricia A. Boyle, PhD, and David A. Bennett, MD

Neurology® 2019;92:e1-e10. doi:10.1212/WNL.0000000000007036

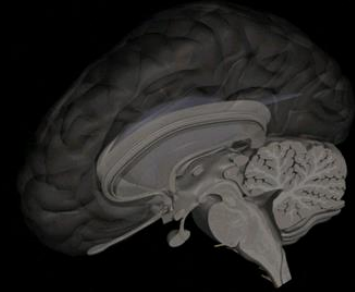
Correspondence
Dr. Wilson
rwilson@rush.edu

Sleep Drives Metabolite Clearance from the Adult Brain

SCIENCE VOL 342 18 OCTOBER 2013

Lulu Xie,^{1*} Hongyi Kang,^{1*} Qiwu Xu,¹ Michael J. Chen,¹ Yonghong Liao,¹ Meenakshisundaram Thiyagarajan,¹ John O'Donnell,¹ Daniel J. Christensen,¹ Charles Nicholson,² Jeffrey J. Iliff,¹ Takahiro Takano,¹ Rashid Deane,¹ Maiken Nedergaard^{1†}

The conservation of sleep across all animal species suggests that sleep serves a vital function. We here report that sleep has a critical function in ensuring metabolic homeostasis. Using real-time assessments of tetramethylammonium diffusion and two-photon imaging in live mice, we show that natural sleep or anesthesia are associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid. In turn, convective fluxes of interstitial fluid increased the rate of β -amyloid clearance during sleep. Thus, the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous



Sleep, clocks, and synaptic plasticity

Marcos G. Frank^{1*} and Rafael Cantera^{2,3*}

¹ Department of Neuroscience, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA

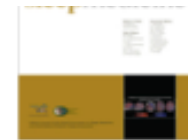
² Zoology Department, Stockholm University, Stockholm, Sweden

³ Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay



Sleep Medicine

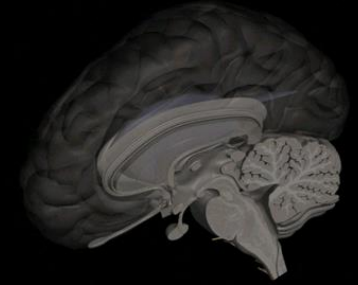
journal homepage: www.elsevier.com/locate/sleep



Original Article

The history of sleep apnea is associated with shorter leukocyte telomere length: the Helsinki Birth Cohort Study

Katri Savolainen^{a,*}, Johan G. Eriksson^{b,c,d,e,f}, Eero Kajantie^{b,g}, Marius Lahti^a, Katri Räikkönen^a



FALTA DE SUEÑO ASOCIADA A:

- MENOR RENDIMIENTO ESCOLAR
- MAYOR IRRITABILIDAD DIURNA
- MENOR SECRECIÓN HcG
- OBESIDAD
- CEFALEA
- SONAMBULISMO Y PESADILLAS
- TRASTORNOS EMOCIONALES Y CONDUCTUALES TARDÍOS
- IDEACIÓN SUICIDA
- ACCIDENTE CEREBROVASCULAR
- ALZHEIMER
- PARKINSON
- EPILEPSIA
- ESCLEROSIS MÚLTIPLE
- JAQUECAS
- DOLOR CRÓNICO
- TRASTORNOS DEL ÁNIMO

COMER BIEN

-OMEGA 3

-PROBIÓTICOS

-DESAYUNAR ABUNDANTEMENTE

-EVITAR AYUNO PROLONGADO

-ESTUDIAR OLIGOELEMENTOS EN DIETAS RESTRICTIVAS

-EVITAR COMIDA CHATARRA



Fang Li, Xiaoqin Liu, Dongfeng Zhang

Li F, et al. *J Epidemiol Community Health* 2015;0:1–6. doi:10.1136/jech-2015-206278

ABSTRACT

Background The association between fish consumption and risk of depression is controversial. We performed a meta-analysis to evaluate the association.

Methods A literature search was performed in PubMed, EMBASE and Web of Science database for all relevant studies up to March 2015. We pooled the relative risks (RRs) with 95% CIs from individual studies with random effects model, and conducted meta-regression to explore potential sources of heterogeneity. Publication bias was estimated by Egger's test and the funnel plot.

Results A total of 26 studies involving 150 278 participants were included in the present meta-analysis. The pooled RR of depression for the highest versus lowest consumption of fish was 0.83 (95% CI 0.74 to 0.93). The findings remained significant in the cohort studies (RR=0.84, 95% CI 0.75 to 0.94, n=10) as well as in the cross-sectional studies (RR=0.82, 95% CI 0.68 to 1.00, n=16). When men and women were analysed separately, a significant inverse association was also observed. There was no evidence of publication bias.

Conclusions This meta-analysis indicates that high-fish consumption can reduce the risk of depression.

structure and function,^{9–10} has been reported to be associated with depression in several studies.^{11–14} However, others did not find an association between fish consumption and depression risk.^{15–19}

Considering the inconsistent and inconclusive findings of the epidemiology studies, we conducted a meta-analysis to summarise the results of observational studies on the association between fish consumption and depression risk.

MATERIALS AND METHODS

We consulted Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for reporting of meta-analyses in this analysis.²⁰

Search strategy

We performed a literature search up to March 2015 in the databases of PubMed, EMBASE and Web of Science, with the following search terms, 'depression' or 'depressive disorder' or 'depressive symptoms' and 'fish'. All searches were limited to studies conducted in humans and published in English. Furthermore, the reference lists of

Low Blood Long Chain Omega-3 Fatty Acids in UK Children Are Associated with Poor Cognitive Performance and Behavior: A Cross-Sectional Analysis from the DOLAB Study

Paul Montgomery*, Jennifer R. Burton, Richard P. Sewell, Thees F. Spreckelsen, Alexandra J. Richardson

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Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity

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BACKGROUND & AIMS: Changes in gut microbiota have been reported to alter signaling mechanisms, emotional behavior, and visceral nociceptive reflexes in rodents. However, alteration of the intestinal microbiota with antibiotics or probiotics has not been shown to produce these changes in humans. We investigated whether consumption of a fermented milk product with probiotic (FMPP) for 4 weeks by healthy women altered brain intrinsic connectivity or responses to emotional attention tasks. **METHODS:** Healthy women with no gastrointestinal or psychiatric symptoms were randomly assigned to groups given FMPP (n = 12), a nonfermented milk product (n = 11, controls), or no intervention (n = 13) twice daily for 4 weeks. The FMPP contained *Bifidobacterium animalis* subsp *Lactis*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp *Lactis*. Participants underwent functional magnetic resonance imaging before and after the intervention to measure brain response to an emotional faces attention task and resting brain activity. Multivariate and region of interest analyses were performed. **RESULTS:** FMPP intake was associated with reduced task-related response of a distributed functional network (49% cross-block covariance; $P = .004$) containing affective, viscerosensory, and somatosensory cortices. Alterations in intrinsic activity of resting brain indicated that ingestion of FMPP was associated with changes in midbrain connectivity, which could explain the observed differences in activity during the task. **CONCLUSIONS:** Four-week intake of an FMPP by healthy women affected activity of brain regions that control central processing of emotion and sensation.

might have a homologous effect on normal human behavior and that alterations in their composition, or in their metabolic products can play a role in the pathophysiology of psychiatric disease or in chronic abdominal pain syndromes, such as irritable bowel syndrome (IBS).^{11–14} However, in contrast to the strong preclinical evidence linking alterations in gut microbiota to emotional behavior, there is only suggestive evidence that a similar relationship might exist in humans.^{3,15–17}

Many reports have provided evidence for effects of probiotics on gut function and visceral sensitivity.^{18,19} For example, various strains of probiotics have been demonstrated to reduce visceral nociceptive reflex responses in rodents and human symptoms of abdominal discomfort; however, the mechanism(s) underlying these effects remain poorly understood.^{8,20–27} In addition to various suggested peripheral mechanisms, alteration in central modulation of interoceptive signals, including the engagement of descending bulbospinal pain modulation systems, or ascending monoaminergic modulation of sensory brain regions, can also play a role.^{28,29} Alterations in such endogenous pain-modulation systems have been implicated in the pathophysiology of persistent pain syndromes, such as IBS and fibromyalgia.^{30–32}

There are many potential signaling mechanisms by which gut microbiota and probiotics could influence brain activity, including changes in microbiota-produced signaling molecules (including amino acid metabolites, short chain fatty acids, and neuroactive substances), mucosal immune mechanisms, and enterochromaffin cell-mediated vagal activation.^{12,33–37} In rodent studies, altered

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ORIGINAL ARTICLES

Soft Drinks Consumption Is Associated with Behavior Problems in 5-Year-Olds

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Objective To examine soda consumption and aggressive behaviors, attention problems, and withdrawal behavior among 5-year-old children.

Study design The Fragile Families and Child Wellbeing Study is a prospective birth cohort study that follows a sample of mother-child pairs from 20 large US cities. Mothers reported children's behaviors using the Child Behavior Checklist at age 5 years and were asked to report how many servings of soda the child drinks on a typical day.

Results In the sample of 2929 children, 52% were boys, 51% were African-American, 43% consumed at least one serving of soda per day, and 4% consumed 4 or more servings per day. In analyses adjusted for sociodemographic factors, consuming one (beta, 0.7; 95% CI, 0.1–1.4), 2 (beta, 1.8; 95% CI, 0.8–2.7), 3 (beta, 2.0; 95% CI, 0.6–3.4), or 4 or more (beta, 4.7; 95% CI, 3.2–6.2) servings was associated with a higher aggressive behavior score compared with consuming no soda. Furthermore, those who consumed 4 or more (beta, 1.7; 95% CI, 1.0–2.4) soda servings had higher scores on the attention problems subscale. Higher withdrawn behavior scores were noted among those consuming 2 (beta, 1.0; 95% CI, 0.3–1.8) or 4 or more (beta, 2.0; 95% CI, 0.8–3.1) soda servings compared with those who consumed no soda.


Conclusion We note an association between soda consumption and negative behavior among very young children; future studies should explore potential mechanisms that could explain this association. (*J Pediatr* 2013; ■: ■–■).

SYSTEMATIC REVIEW

Open Access



Physical Activity on Telomere Length as a Biomarker for Aging: A Systematic Review

Marlies Schellnegger^{1,2,3*} , Alvin C. Lin^{3*}, Niels Hammer³ and Lars-Peter Kamolz^{1,2}

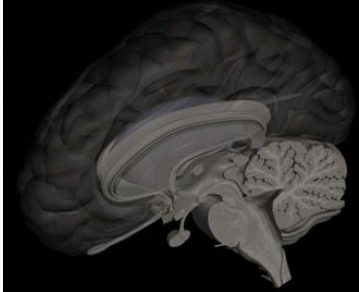
Abstract

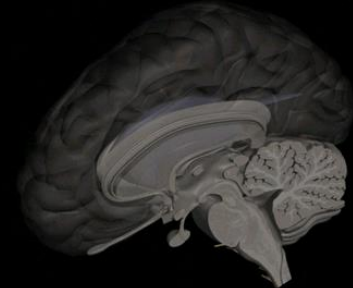
Background: Overall life expectancy continues to rise, approaching 80 years of age in several developed countries. However, healthy life expectancy lags far behind, which has, in turn, contributed to increasing costs in healthcare. One way to improve health and attenuate the socio-economic impact of an aging population is to increase overall fitness through physical activity. Telomere attrition or shortening is a well-known molecular marker in aging. As such, several studies have focused on whether exercise influences health and aging through telomere biology. This systematic review examines the recent literature on the effect of physical activity on telomere length (TL) and/or telomerase activity as molecular markers of aging.

Methods: A focused search was performed in the databases PubMed and Web of Science for retrieving relevant articles over the past ten years. The search contained the following keywords: exercise, sport, physical activity, fitness, sedentary, physical inactivity, telomere, telomere length, t/s ratio, and telomerase. PRISMA guidelines for systematic reviews were observed.

Results: A total of 43 articles were identified and categorized into randomized controlled trials (RCT), observational or interventional studies. RCTs ($n = 8$) showed inconsistent findings of increased TL length with physical activity in, e.g. obese, post-menopausal women. In comparison with a predominantly sedentary lifestyle, observational studies ($n = 27$) showed significantly longer TL with exercise of moderate to vigorous intensity; however, there was no consensus on the duration and type of physical activity and training modality. Interventional studies ($n = 8$) also showed similar findings of significantly longer TL prior to exercise intervention; however, these studies had smaller numbers of enrolled participants (mostly of high-performance athletes), and the physical activities covered a range of exercise intensities and duration. Amongst the selected studies, aerobic training of moderate to vigorous intensity is most prevalent. For telomere biology analysis, TL was determined mainly from leukocytes using qPCR. In some cases, especially in RCT and interventional studies, different sample types such as saliva, sperm, and muscle biopsies were analyzed; different leukocyte cell types and potential genetic markers in regulating telomere biology were also investigated.

Conclusions: Taken together, physical activity with regular aerobic training of moderate to vigorous intensity appears to help preserve TL. However, the optimal intensity, duration of physical activity, as well as type of exercise





Effects of the FITKids Randomized Controlled Trial on Executive Control and Brain Function

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KEY WORDS

cognition, physical activity, aerobic fitness, randomized controlled trial

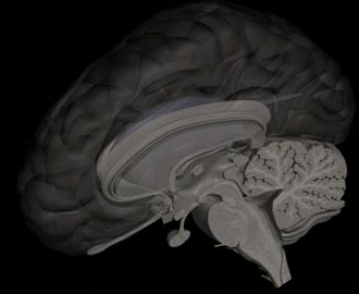


WHAT'S KNOWN ON THIS SUBJECT: Physical activity programs have been shown to have positive implications for children's cognitive performance and brain structure and function. However, additional randomized controlled trials are needed to determine whether daily physical activity influences executive control and its neural underpinnings.



WHAT THIS STUDY ADDS: The randomized controlled trial, designed to meet daily physical activity recommendations, used behavioral and electrophysiological measures of brain function to demonstrate enhanced attentional inhibition and cognitive flexibility among prepubertal children.

Pediatrics 2014;134:e1063–e1071



Systems/Circuits

Older Adults Benefit from Music Training Early in Life: Biological Evidence for Long-Term Training-Driven Plasticity

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Aging results in pervasive declines in nervous system function. In the auditory system, these declines include neural timing delays in response to fast-changing speech elements; this causes older adults to experience difficulty understanding speech, especially in challenging listening environments. These age-related declines are not inevitable, however: older adults with a lifetime of music training do not exhibit neural timing delays. Yet many people play an instrument for a few years without making a lifelong commitment. Here, we examined neural timing in a group of human older adults who had nominal amounts of music training early in life, but who had not played an instrument for decades. We found that a moderate amount (4–14 years) of music training early in life is associated with faster neural timing in response to speech later in life, long after training stopped (>40 years). We suggest that early music training sets the stage for subsequent interactions with sound. These experiences may interact over time to sustain sharpened neural processing in central auditory nuclei well into older age.

Behavioral and Neural Correlates of Executive Functioning in Musicians and Non-Musicians

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Abstract

Executive functions (EF) are cognitive capacities that allow for planned, controlled behavior and strongly correlate with academic abilities. Several extracurricular activities have been shown to improve EF, however, the relationship between musical training and EF remains unclear due to methodological limitations in previous studies. To explore this further, two experiments were performed; one with 30 adults with and without musical training and one with 27 musically trained and untrained children (matched for general cognitive abilities and socioeconomic variables) with a standardized EF battery. Furthermore, the neural correlates of EF skills in musically trained and untrained children were investigated using fMRI. Adult musicians compared to non-musicians showed enhanced performance on measures of cognitive flexibility, working memory, and verbal fluency. Musically trained children showed enhanced performance on measures of verbal fluency and processing speed, and significantly greater activation in pre-SMA/SMA and right VLPFC during rule representation and task-switching compared to musically untrained children. Overall, musicians show enhanced performance on several constructs of EF, and musically trained children further show heightened brain activation in traditional EF regions during task-switching. These results support the working hypothesis that musical training may promote the development and maintenance of certain EF skills, which could mediate the previously reported links between musical training and enhanced cognitive skills and academic achievement.

Citation: Zuk J, Benjamin C, Kenyon A, Gaab N (2014) Behavioral and Neural Correlates of Executive Functioning in Musicians and Non-Musicians. PLoS ONE 9(6): e99868. doi:10.1371/journal.pone.0099868

Editor: Amanda Bruce, University of Missouri-Kansas City, United States of America

Received: December 31, 2013; **Accepted:** May 20, 2014; **Published:** June 17, 2014



Taming a wandering attention: Short-form mindfulness training in student cohorts

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Reviewed by:

Vernon Anthony Barnes, Georgia Health Sciences University, USA

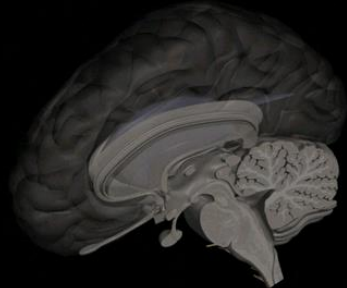
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Mindfulness training (MT) is a form of mental training in which individuals engage in exercises to cultivate an attentive, present centered, and non-reactive mental mode. The present study examines the putative benefits of MT in University students for whom mind wandering can interfere with learning and academic success. We tested the hypothesis that short-form MT (7 h over 7 weeks) contextualized for the challenges and concerns of University students may reduce mind wandering and improve working memory. Performance on the sustained attention to response task (SART) and two working memory tasks (operation span, delayed-recognition with distracters) was indexed in participants assigned to a waitlist control group or the MT course. Results demonstrated MT-related benefits in SART performance. Relative to the control group, MT participants had higher task accuracy and self-reported being more “on-task” after the 7-week training period. MT did not significantly benefit the operation span task or accuracy on the delayed-recognition task. Together these results suggest that while short-form MT did not bolster working memory task performance, it may help curb mind wandering and should, therefore, be further investigated for its use in academic contexts.



POLICY STATEMENT

Literacy Promotion: An Essential Component of Primary Care Pediatric Practice

COUNCIL ON EARLY CHILDHOOD

KEY WORDS

literacy promotion, reading aloud, early brain development, language development, child development, school readiness

ABBREVIATIONS

AAP—American Academy of Pediatrics
ROR—Reach Out and Read

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abstract

FREE

Reading regularly with young children stimulates optimal patterns of brain development and strengthens parent-child relationships at a critical time in child development, which, in turn, builds language, literacy, and social-emotional skills that last a lifetime. Pediatric providers have a unique opportunity to encourage parents to engage in this important and enjoyable activity with their children beginning in infancy. Research has revealed that parents listen and children learn as a result of literacy promotion by pediatricians, which provides a practical and evidence-based opportunity to support early brain development in primary care practice. The American Academy of Pediatrics (AAP) recommends that pediatric providers promote early literacy development for children beginning in infancy and continuing at least until the age of kindergarten entry by (1) advising all parents that reading aloud with young children can enhance parent-child relationships and prepare young minds to learn language and early literacy skills; (2) counseling all parents about developmentally appropriate shared-reading activities that are enjoyable for children and their parents and offer language-rich exposure to books, pictures, and the written word; (3) providing developmentally appropriate books given at health supervision visits for all high-risk, low-income young children; (4) using a robust spectrum of options to support and promote these efforts; and (5) partnering with other child advocates to influence national messaging and policies that support and promote these key early shared-reading experiences. The AAP supports federal and state funding for children's books to be provided at pediatric health supervision visits to children at high risk living at or near the poverty threshold and the integration of literacy promotion, an essential component of pediatric primary care, into pediatric resident education. This policy statement is supported by the AAP technical report "School Readiness" and supports the AAP policy statement "Early Childhood Adversity, Toxic Stress, and the Role of the Pediatrician: Translating Developmental Science into Lifelong Health." *Pediatrics* 2014;134:1-6



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Reading linear texts on paper versus computer screen: Effects on reading comprehension

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ARTICLE INFO

Article history:
Received 24 May 2012
Received in revised form 6 December 2012
Accepted 10 December 2012
Available online 5 January 2013

Keywords:
Reading comprehension
Screen reading
Print reading
Computers in education

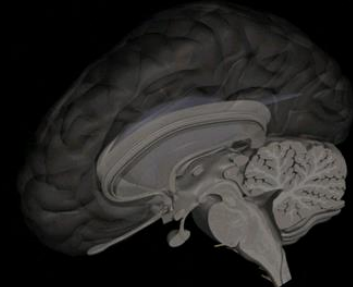
ABSTRACT

Objective: To explore effects of the technological interface on reading comprehension in a Norwegian school context.

Participants: 72 tenth graders from two different primary schools in Norway.

Method: The students were randomized into two groups, where the first group read two texts (1400–2000 words) in print, and the other group read the same texts as PDF on a computer screen. In addition pretests in reading comprehension, word reading and vocabulary were administered. A multiple regression analysis was carried out to investigate to what extent reading modality would influence the students' scores on the reading comprehension measure.

Conclusion: Main findings show that students who read texts in print scored significantly better on the reading comprehension test than students who read the texts digitally. Implications of these findings for policymaking and test development are discussed.



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



FlashReport

The more you play, the more aggressive you become: A long-term experimental study of cumulative violent video game effects on hostile expectations and aggressive behavior

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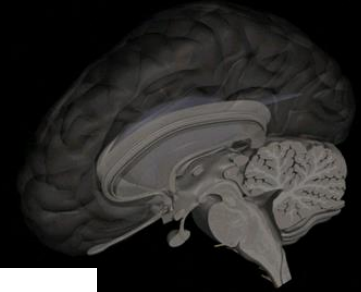
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HIGHLIGHTS

- ▶ A 3-day experiment tested the cumulative effects of violent video games.
- ▶ Hostile expectations increased over 3 days for violent video game players.
- ▶ Aggression increased over 3 days for violent video game players.
- ▶ Hostile expectations mediated the effect of violent video games on aggression.
- ▶ Nonviolent video games did not influence hostile expectations or aggression.



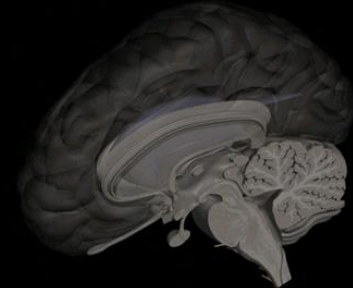
Differences in Parent-Toddler Interactions With Electronic Versus Print Books

Tiffany G. Munzer, MD,^a Alison L. Miller, PhD,^{b,c} Heidi M. Weeks, PhD,^d Niko Kaciroti, PhD,^{c,e} Jenny Radesky, MD^a

WHAT'S KNOWN ON THIS SUBJECT: When preschoolers read electronic books with parents, parents may show less dialogic reading, and talk is often focused on the technology. It is not known whether toddler-parent interactions differ when reading commercially available electronic books compared with print.

WHAT THIS STUDY ADDS: Parents engaged in more dialogic reading with fewer technology-related verbalizations and more parent-toddler verbalizations with print books compared with electronic books. Print books elicited a higher quality of parent-toddler collaborative reading experience compared with electronic books.

To cite: Munzer TG, Miller AL, Weeks HM, et al. Differences in Parent-Toddler Interactions With Electronic Versus Print Books. *Pediatrics*. 2019;143(4):e20182012

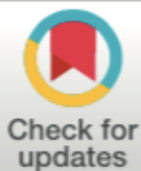


RESEARCH ARTICLE

Screen-time is associated with inattention problems in preschoolers: Results from the CHILD birth cohort study

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Check for updates

Direct Effect of Sunshine on Suicide

Benjamin Vyssoki, MD; Nestor D. Kapusta, MD, PhD; Nicole Praschak-Rieder, MD, PhD;
Georg Dorffner, PhD; Matthaeus Willeit, MD, PhD

IMPORTANCE It has been observed that suicidal behavior is influenced by sunshine and follows a seasonal pattern. However, seasons bring about changes in several other meteorological factors and a seasonal rhythm in social behavior may also contribute to fluctuations in suicide rates.

OBJECTIVE To investigate the effects of sunshine on suicide incidence that are independent of seasonal variation.

DESIGN, SETTING, AND PARTICIPANTS Retrospective analysis of data on all officially confirmed suicides in Austria between January 1, 1970, and May 6, 2010 ($n = 69\ 462$). Data on the average duration of sunshine per day (in hours) were calculated from 86 representative meteorological stations. Daily number of suicides and daily duration of sunshine were differentiated to remove variation in sunshine and variation in suicide incidence introduced by season. Thereafter, several models based on Pearson correlation coefficients were calculated.

MAIN OUTCOMES AND MEASURES Correlation of daily number of suicides and daily duration of sunshine after mathematically removing the effects of season.

RESULTS Sunshine hours and number of suicides on every day from January 1, 1970, to May 6, 2010, were highly correlated ($r = 0.4870$; $P < 10^{-9}$). After differencing for the effects of season, a mathematical procedure that removes most of the variance from the data, a positive correlation between number of suicides and hours of daily sunshine remained for the day of suicide and up to 10 days prior to suicide ($r_{\text{maximum}} = 0.0370$; $P < 10^{-5}$). There was a negative correlation between the number of suicides and daily hours of sunshine for the 14 to 60 days prior to the suicide event ($r_{\text{minimum}} = -0.0383$; $P < 10^{-5}$). These effects were found in the entire sample and in violent suicides.

CONCLUSIONS AND RELEVANCE Duration of daily sunshine was significantly correlated with suicide frequency independent of season, but effect sizes were low. Our data support the hypothesis that sunshine on the day of suicide and up to 10 days prior to suicide may facilitate suicide. More daily sunshine 14 to 60 days previously is associated with low rates of suicide. Our study also suggests that sunshine during this period may protect against suicide.

Effect of Time Spent Outdoors at School on the Development of Myopia Among Children in China A Randomized Clinical Trial

Mingguang He, MD, PhD; Fan Xiang, MD, PhD; Yangfa Zeng, MD; Jincheng Mai, BSc; Qiayun Chen, MSc;
Jian Zhang, MSc; Wayne Smith, MD, PhD; Kathryn Rose, PhD; Ian G. Morgan, PhD

IMPORTANCE Myopia has reached epidemic levels in parts of East and Southeast Asia. However, there is no effective intervention to prevent the development of myopia.

OBJECTIVE To assess the efficacy of increasing time spent outdoors at school in preventing incident myopia.

DESIGN, SETTING, AND PARTICIPANTS Cluster randomized trial of children in grade 1 from 12 primary schools in Guangzhou, China, conducted between October 2010 and October 2013.

INTERVENTIONS For 6 intervention schools ($n = 952$ students), 1 additional 40-minute class of outdoor activities was added to each school day, and parents were encouraged to engage their children in outdoor activities after school hours, especially during weekends and holidays. Children and parents in the 6 control schools ($n = 951$ students) continued their usual pattern of activity.

MAIN OUTCOMES AND MEASURES The primary outcome measure was the 3-year cumulative incidence rate of myopia (defined using the Refractive Error Study in Children spherical equivalent refractive error standard of ≤ -0.5 diopters [D]) among the students without established myopia at baseline. Secondary outcome measures were changes in spherical equivalent refraction and axial length among all students, analyzed using mixed linear models and intention-to-treat principles. Data from the right eyes were used for the analysis.

RESULTS There were 952 children in the intervention group and 951 in the control group with a mean (SD) age of 6.6 (0.34) years. The cumulative incidence rate of myopia was 30.4% in the intervention group (259 incident cases among 853 eligible participants) and 39.5% (287 incident cases among 726 eligible participants) in the control group (difference of -9.3% [95% CI, -14.1% to -4.1%]; $P < .001$). There was also a significant difference in the 3-year change in spherical equivalent refraction for the intervention group (-1.42 D) compared with the control group (-1.59 D) (difference of 0.17 D [95% CI, 0.01 to 0.33 D]; $P = .04$). Elongation of axial length was not significantly different between the intervention group (0.95 mm) and the control group (0.98 mm) (difference of -0.03 mm [95% CI, -0.07 to 0.003 mm]; $P = .07$).

CONCLUSIONS AND RELEVANCE Among 6-year-old children in Guangzhou, China, the addition of 40 minutes of outdoor activity at school compared with usual activity resulted in a reduced incidence rate of myopia over the next 3 years. Further studies are needed to assess long-term follow-up of these children and the generalizability of these findings.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00848900

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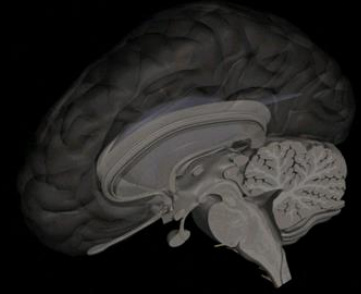
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CME Questions page 1173

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Trends in Intracranial and Cerebral Volumes of Framingham Heart Study Participants Born 1930 to 1970

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IMPORTANCE Human brain development and maintenance is under both genetic and environmental influences that likely affect later-life dementia risk.

OBJECTIVE To examine environmental influences by testing whether time-dependent secular differences occurred in cranial and brain volumes and cortical thickness over birth decades spanning 1930 to 1970.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study used data from the community-based Framingham Heart Study cohort for participants born in the decades 1930 to 1970. Participants did not have dementia or history of stroke and had magnetic resonance imaging (MRI) obtained from March 18, 1999, to November 15, 2019. The final analysis dataset was created in October 2023.

EXPOSURE Years of birth ranging from 1925 to 1968.

MAIN MEASURES Cross-sectional analysis of intracranial, cortical gray matter, white matter, and hippocampal volumes as well as cortical surface area and cortical thickness. The secular measure was the decade in which the participant was born. Covariates included age at MRI and sex.

RESULTS The main study cohort consisted of 3226 participants with a mean (SD) age of 57.7 (7.8) years at the time of their MRI. A total of 1706 participants were female (53%) and 1520 (47%) were male. The birth decades ranged from the 1930s to 1970s. Significant trends for larger intracranial, hippocampal, and white matter volumes and cortical surface area were associated with progressive birth decades. Comparing the 1930s birth decade to the 1970s accounted for a 6.6% greater volume (1234 mL; 95% CI, 1220-1248, vs 1321 mL; 95% CI, 1301-1341) for ICV, 7.7% greater volume (441.9 mL; 95% CI, 435.2-448.5, vs 476.3 mL; 95% CI, 467.0-485.7) for white matter, 5.7% greater value (6.51 mL; 95% CI, 6.42-6.60, vs 6.89 mL; 95% CI, 6.77-7.02) for hippocampal volume, and a 14.9% greater value (1933 cm²; 95% CI, 1908-1959, vs 2222 cm²; 95% CI, 2186-2259) for cortical surface area. Repeat analysis applied to a subgroup of 1145 individuals of similar age range born in the 1940s (mean [SD] age, 60.0 [2.8] years) and 1950s (mean [SD] age, 59.0 [2.8] years) resulted in similar findings.

CONCLUSION AND RELEVANCE In this study, secular trends for larger brain volumes suggested improved brain development among individuals born between 1930 and 1970. Early life environmental influences may explain these results and contribute to the declining dementia incidence previously reported in the Framingham Heart Study cohort.

+ Editorial

+ Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Charles DeCarli, MD, Department of Neurology, University of California Davis, 4860 Y St, Ste 3700, Sacramento, CA 95817 (cdecarli@ucdavis.edu).

COGNITIVE DEVELOPMENT

Infants make more attempts to achieve a goal when they see adults persist

Julia A. Leonard,* Yuna Lee, Laura E. Schulz

Persistence, above and beyond IQ, is associated with long-term academic outcomes. To look at the effect of adult models on infants' persistence, we conducted an experiment in which 15-month-olds were assigned to one of three conditions: an Effort condition in which they saw an adult try repeatedly, using various methods, to achieve each of two different goals; a No Effort condition in which the adult achieved the goals effortlessly; or a Baseline condition. Infants were then given a difficult, novel task. Across an initial study and two preregistered experiments ($N = 262$), infants in the Effort condition made more attempts to achieve the goal than did infants in the other conditions. Pedagogical cues modulated the effect. The results suggest that adult models causally affect infants' persistence and that infants can generalize the value of persistence to novel tasks.

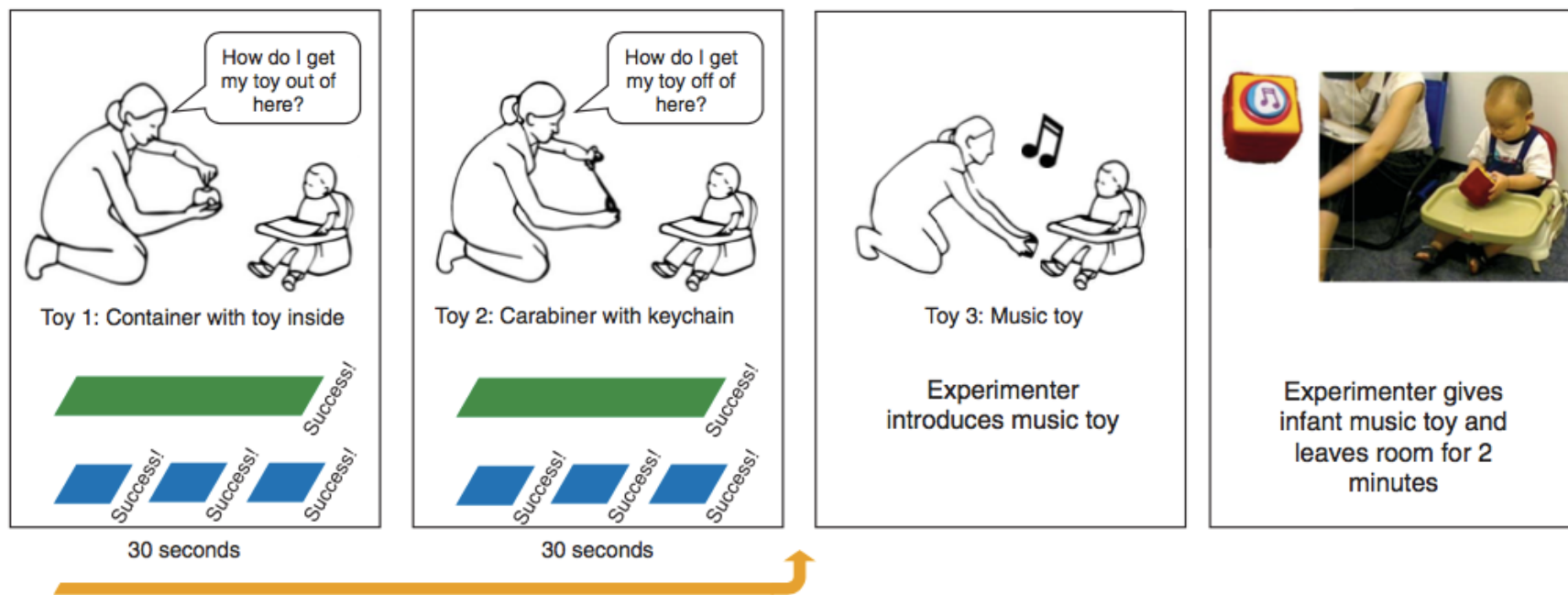
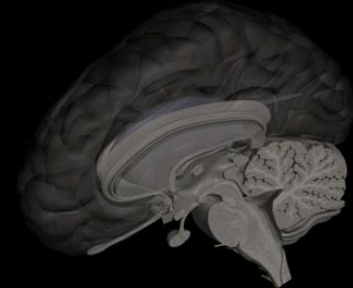
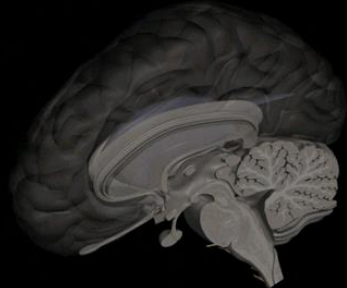
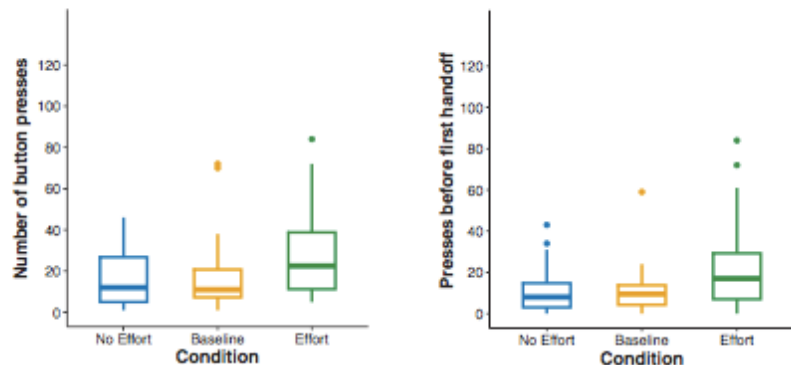


Fig. 1. Schematic of study design. In experiment 1, infants were assigned to one of three conditions: Effort, No Effort, or Baseline. In the Effort condition, the experimenter struggled for 30 s before achieving each of two goals. In the No Effort condition, the experimenter achieved her goals effortlessly three times over 30 s. In the Baseline condition, there was no

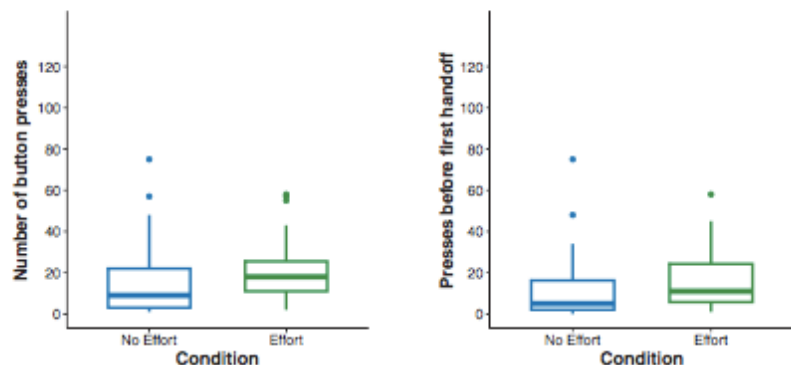
experimenter demonstration. The experimenter then introduced the infant to a novel toy, activated the toy out of the infant's sight so that it played a tune for 5 s, gave the infant the toy, and left the room for 2 min. The dependent variables were the number of times that infants pressed the large (inert) button on the music toy in total and before the first handoff.



Experiment 1



Replication



Experiment 2

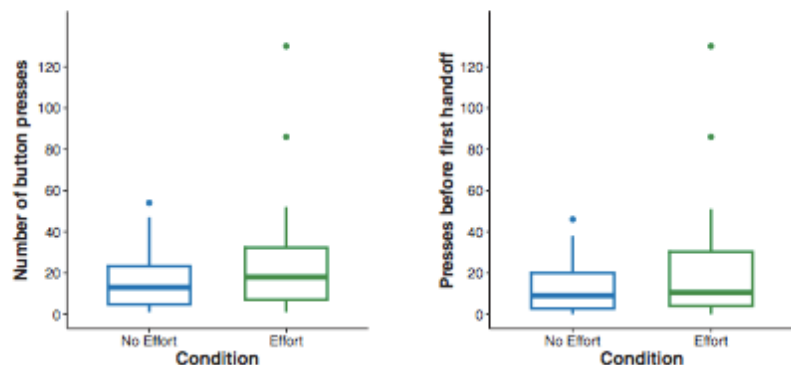


Fig. 2. Results from experiment 1, the replication, and experiment 2. The top and the bottom of the box correspond to the first and third quartiles (the 25th and 75th percentiles). The upper whisker (vertical line) extends from the third quartile to the largest value no further than 1.5 interquartile ranges from the third quartile; the lower whisker extends from the 25th percentile down to the smallest value no further than 1.5 interquartile ranges from the first quartile (i.e., the largest and smallest values that are not outliers). The dots are values more than 1.5 times the interquartile range above the third quartile (outliers). See text for statistical analyses.

1236 22 SEPTEMBER 2017 • VOL 357 ISSUE 6357 **SCIENCE**

HUMAN DEVELOPMENT

The social origins of persistence

Infants can learn the value of persistence by observing adult behavior

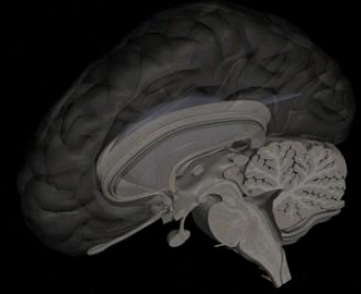
By **Lucas P. Butler**

Effort and hard work have long been regarded as key to achievement and success. But individuals hold different beliefs about how important effort is in determining success, relative to pure talent or natural skill. Recent research has shown that holding a growth mindset—that is, a set of beliefs that em-

was pressed. Unknown to the children, this toy was disabled. The researchers tracked how many times infants tried to activate the toy when given the chance to do so on their own. The results were clear. Infants tried harder when they had seen an adult persist to succeed, relative to both a low-effort and a baseline condition, suggesting that they had drawn the inference that hard work pays off.



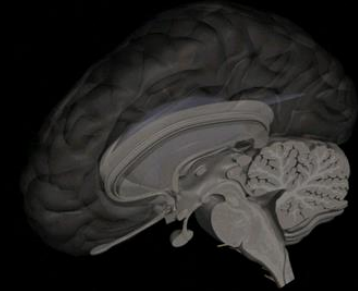
**POR LO TANTO...SE REFUERZA LA IMPORTANCIA DEL ROL
PROMOTOR DE LA SALUD
FÍSICA Y MENTAL EN LA INFANCIA...Y PARA TODA LA VIDA**



TÓPICOS ESPECÍFICOS DE NEUROLOGÍA
DESARROLLO PSICOMOTOR Y APRENDIZAJE

Competencias en lectura, matemáticas y resolución de problemas, por países

Según el estudio PIAAC Ciclo 2 de 2023 entre adultos de entre 16 y 65 años de 31 países y economías



Lectura		Matemáticas		Resolución de problemas	
Finlandia	296	Finlandia	294	Finlandia	276
Japón	289	Japón	291	Japón	276
Suecia	284	Suecia	285	Suecia	273
Noruega	281	Noruega	285	Noruega	271
P. Bajos	279	P. Bajos	284	P. Bajos	265
Estonia	276	Estonia	281	Dinamarca	264
Bélgica ¹	275	Bélgica ¹	279	Estonia	263
Dinamarca	273	Dinamarca	279	Bélgica ¹	262
Inglaterra	272	Suiza	276	Alemania	261
Canadá	271	Singapur	274	Inglaterra	259
Suiza	266	Alemania	273	Canadá	259
Alemania	266	Canadá	271	Suiza	257
Irlanda	263	Inglaterra	268	Austria	253
Chequia	260	Chequia	267	Singapur	252
N. Zelanda	260	Austria	267	Chequia	250
EEUU	258	Letonia	263	Irlanda	249
Francia	255	Eslovaquia	261	N. Zelanda	249
Singapur	254	Irlanda	260	Francia	248
Austria	254	Francia	257	EEUU	247
Eslovaquia	254	N. Zelanda	256	Eslovaquia	247
Croacia	254	Croacia	254	Letonia	244
Corea	249	Hungría	254	Hungría	241
Letonia	248	Corea	253	España	241
Hungría	248	España	250	Corea	238
España	247	EEUU	249	Israel	236
Italia	245	Israel	246	Croacia	235
Israel	244	Lituania	246	Portugal	233
Lituania	238	Italia	244	Italia	231
Polonia	236	Polonia	239	Lituania	230
Portugal	235	Portugal	238	Polonia	226
Chile	218	Chile	214	Chile	218

TADI (TEST DE APRENDIZAJE Y DESARROLLO INFANTIL)

-EVALUACIÓN DESARROLLO Y APRENDIZAJE ENTRE 3 M Y 6 AÑOS DE EDAD

-DISEÑADO Y ESTANDARIZADO EN CHILE

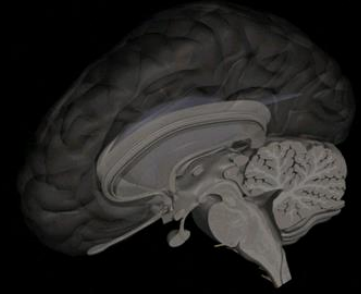
-EVALÚA 4 DIMENSIONES:

COGNICIÓN
LENGUAJE

MOTRICIDAD
SOCIOEMOCIONALIDAD

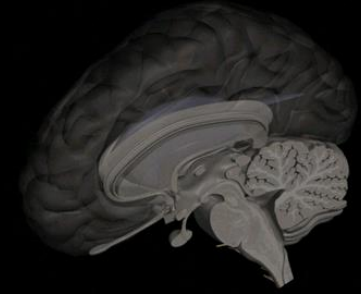


PUNTOS CRÍTICOS



- NIVEL INTELECTUAL MEDIDO POR TEST PSICOMÉTRICOS A LOS 6 AÑOS DE EDAD, ES HABITUALMENTE EL QUE LE ACOMPAÑARÁ TODA SU VIDA
- EL DESARROLLO PSICOMOTOR MEDIDO A LOS 2 AÑOS DE EDAD YA MARCA UNA DIFERENCIA SIGNIFICATIVA SEGÚN EL ORIGEN SOCIO-ECONÓMICO
- FUNDAMENTAL IDENTIFICAR TEMPRANAMENTE GRUPOS O INDIVIDUOS DE RIESGO

RETRASO MOTOR



-BIOLÓGICO

-ESCASA PARTICIPACIÓN DE ESTIMULACIÓN AMBIENTAL

-AVERIGUAR MOVIMIENTOS FETALES

-ALTA ASOCIACIÓN CON ALTERACIONES TONO MOTOR

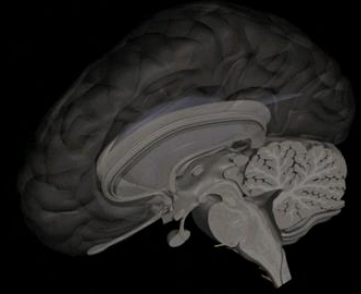
-DESARROLLO MOTOR NORMAL NO IMPLICA INTELIGENCIA NORMAL

-NO SE ASOCIA A PESO O SER CONSENTIDO

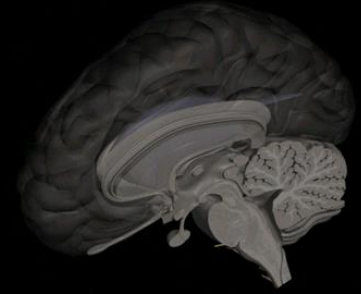
-RANGO DE VARIABILIDAD Y LÍMITES DE NORMALIDAD

-SIEMPRE DESCARTAR MIOPATÍAS CON CK

RETRASO DE LENGUAJE



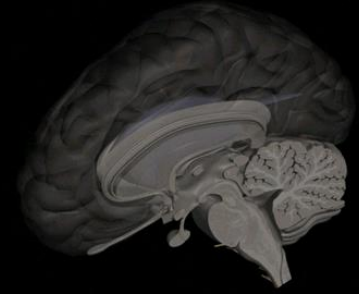
- MAYOR DEPENDENCIA DE ESTIMULACIÓN
- REQUIERE INDEMNIDAD SENSORIAL
- MAYOR CORRELATO CON DESARROLLO COGNITIVO
VALOR PRONÓSTICO PARA APRENDIZAJE ESCOLAR
- ETAPA PREVERBAL DEL LENGUAJE
- HALLAZGO HABITUAL RETROSPECTIVO EN RETARDO MENTAL
- ELEMENTO CENTRAL DE TRASTORNOS DEL ESPECTRO AUTISTA:
ASOCIADO A COMPROMISO DE LA COMUNICACIÓN SOCIAL Y CONDUCTAS
ESPECIALES
- PÉRDIDA DE LENGUAJE: REGRESIÓN AUTÍSTICA-EPILEPSIA-
DETERIORO POR ENFERMEDADES NEURODEGENERATIVAS
- ALTERACIONES “NORMALES” DEL LENGUAJE: TARTAMUDEZ
- SIEMPRE DESCARTAR HIPOACUSIA Y TEA



TÓPICOS ESPECÍFICOS DE NEUROLOGÍA

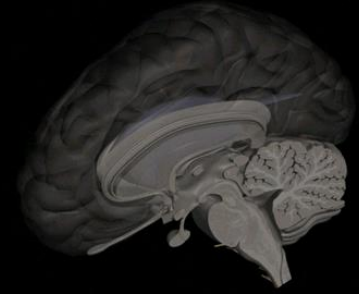
ESTUDIOS ETIOLÓGICOS DE TRASTORNOS DEL
NEURODESARROLLO

PUNTOS CRÍTICOS



- ESTUDIOS NEUROIMÁGENES (TAC-RMN) MUY BAJA EFECTIVIDAD
- ESTUDIOS EEG SOLO SON ÚTILES EN LA SOSPECHA DE EPILEPSIA
- ESTUDIOS METABÓLICOS SON IMPORTANTES SI LA SOSPECHA CLÍNICA ESTÁ FUNDADA, PERO BAJA TASA DE RESULTADOS (ÚTIL COMO SCREENING)
- ESTUDIOS GENÉTICOS SON LA HERRAMIENTA DE MAYOR UTILIDAD

PUNTOS CRÍTICOS



-QUÉ CONDICIONES AMERITAN PLANTEAR ESTUDIO GENÉTICO:

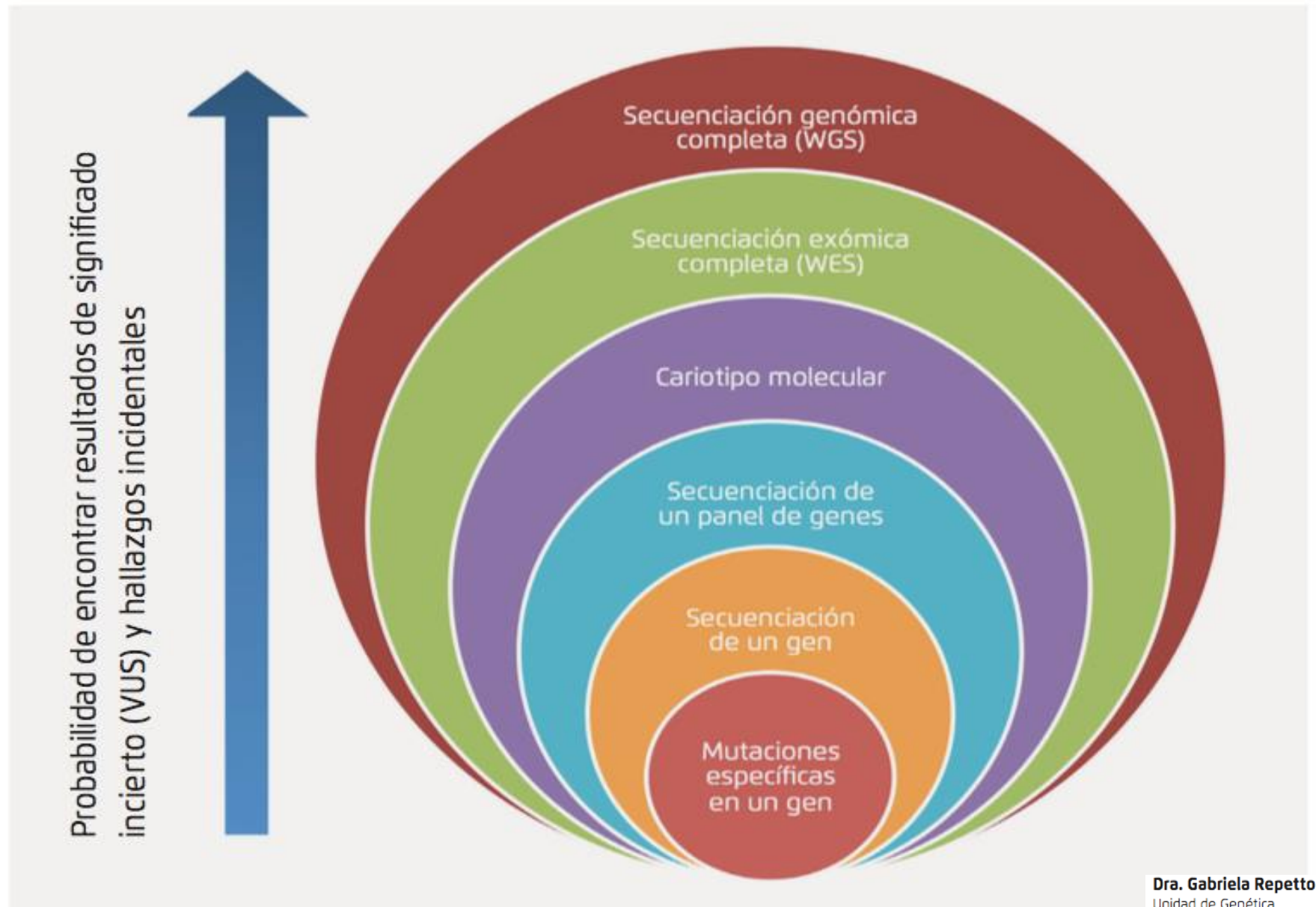
-RETRASO MOTOR + EXAMEN FÍSICO SIN FOCALIDAD
+ ASPECTO DISMÓRFICO

(CON FOCALIDAD: NEUROIMÁGENES)

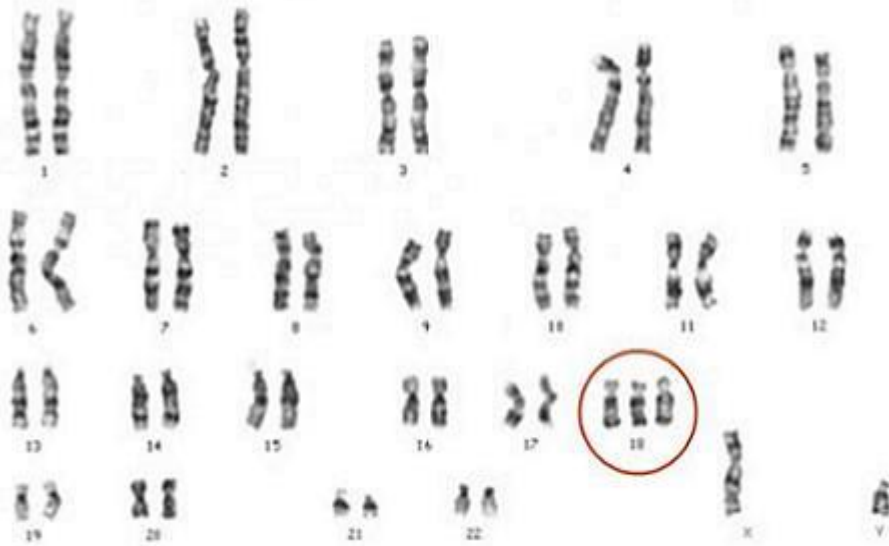
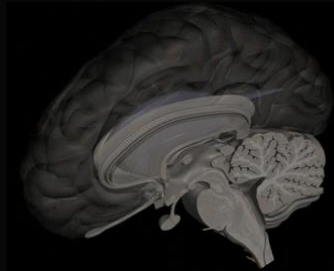
-TRASTORNOS DEL NEURODESARROLLO SEVEROS (TEA) O
ASOCIADOS A EPILEPSIA O COMPROMISO DE OTROS SISTEMAS

-SÍNDROMES DISMÓRFICOS

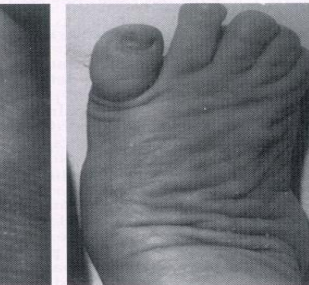
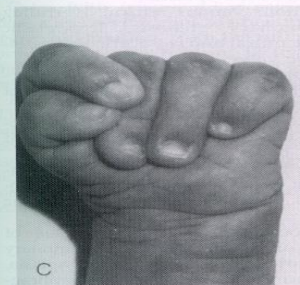
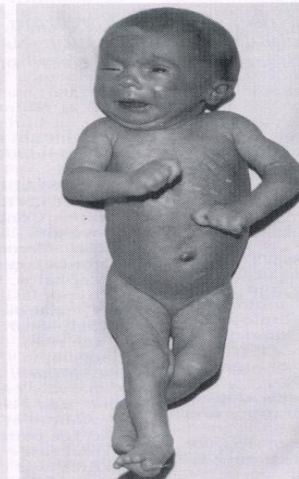
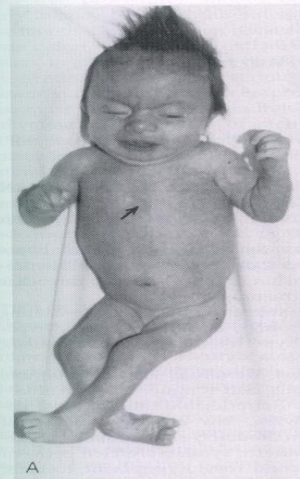
Figura 2. Tipos de tests genéticos, según su complejidad (basado en <http://www.ashg.org/education/images/infographics/testing-purpose.png>)



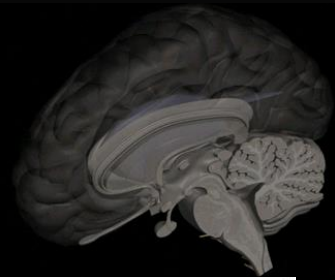
CARIOGRAMA CROMOSOMOPATÍAS: ALTERACIONES NUMÉRICAS



Ideograma de una célula humana de una persona con Síndrome de Edwards, trisomía del par 18.



SÍNDROME DE EDWARD $47,XY(XX)+18$
TRISOMÍA MÁS FRECUENTE ENTRE LOS RN FALLECIDOS MALFORMADOS
RCIU, MICROCEFALIA, CARDIOPATÍA, DEDOS MONTADOS, HIPERTONÍA,
MALFORMACIONES RENALES O INTESTINALES
MAL PRONÓSTICO VITAL



GENOPATÍAS POR DELECCIÓN-DUPLICACIÓN

GENES ESPECÍFICOS: FISH-MLPA-MICROARRAY (CARIOTIPO MOLECULAR)

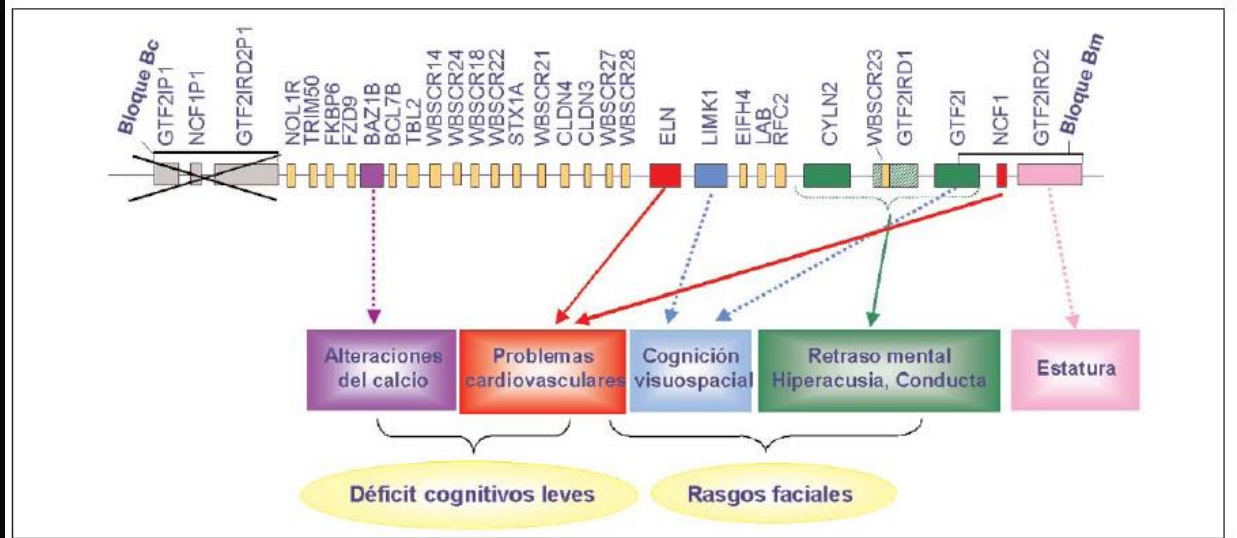
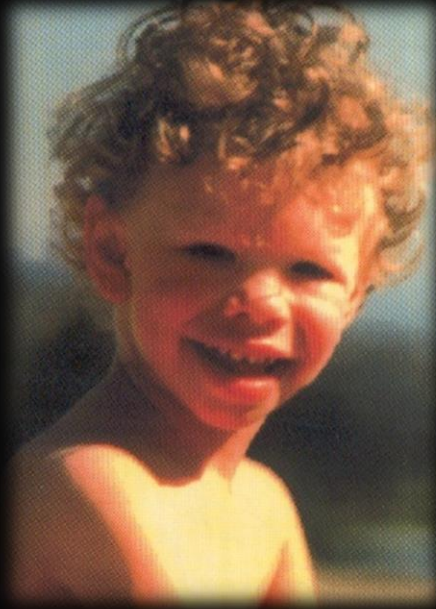
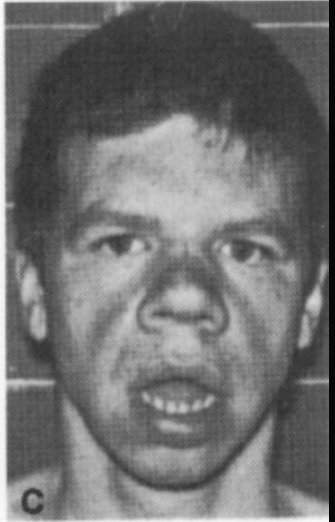


Figura 2. Mapa con los genes de la región 7q11.23 que se pierden en la deleción causante del síndrome de Williams y relación de los más relevantes con los rasgos del fenotipo en los que potencialmente participan. Las flechas continuas implican efectos claramente confirmados, mientras que las flechas discontinuas implican efectos probables.



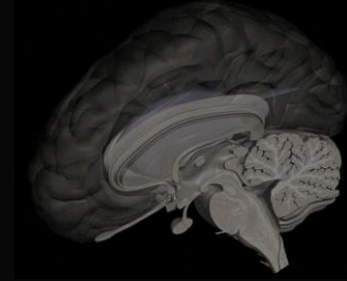
NORMAL

SW



SÍNDROME DE WILLIAMS c.7 (*genes contíguos*)

ALTERACIONES GENÉTICAS POR MUTACIONES DENTRO DE UN GEN ESPECÍFICO NGS (PANELES GENÉTICOS)



PANEL EPILEPSIA
(300 GENES)

“PESADILLAS
DE LAS VUS”



RESULT: POSITIVE

One Pathogenic variant identified in **GNAO1**. **GNAO1** is associated with a spectrum of autosomal dominant conditions including epilepsy and involuntary movements.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
GNAO1	c.625C>T (p.Arg209Cys)	heterozygous	PATHOGENIC
CACNA1H	c.1609C>T (p.Arg537Cys)	heterozygous	Uncertain Significance
GAMT	c.22C>A (p.Pro8Thr)	heterozygous	Uncertain Significance
JMJD1C	c.4421C>T (p.Ser1474Leu)	heterozygous	Uncertain Significance
RELN	c.3667A>G (p.Lys1223Glu)	heterozygous	Uncertain Significance

About this test

This diagnostic test evaluates 189 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Clinical Summary

A Pathogenic variant, c.625C>T (p.Arg209Cys), was identified in **GNAO1**.

- The **GNAO1** gene is associated with an autosomal dominant spectrum of conditions including early infantile epileptic encephalopathy (EIEE) (MedGen UID: 815936) and neurodevelopmental disorder with involuntary movements (NEDIM) (MedGen UID: 1374697).
- This result is consistent with a predisposition to, or diagnosis of, **GNAO1**-related conditions.
- Early infantile epileptic encephalopathies are profound seizure disorders with onset at or soon after birth (PMID: 22548976, 23027099). They can present with a variety of seizures that may occur up to hundreds of times a day and independent of the sleep cycle. Affected individuals may also present with hypotonia, cognitive and motor impairment, and other anomalies (PMID: 22548976, 23027099). NEDIM is a neurodevelopmental disorder characterized by psychomotor delay and childhood onset of involuntary movements including dystonia, athetosis, and chorea (PMID: 25966631, 27068059).

ALTERACIONES GENÉTICAS ESTUDIO POR SECUENCIACIÓN COMPLETA DEL EXOMA



Prueba(s) solicitada(s): CentoXome® Solo (secuenciación NGS y análisis de CNV)

INFORMACIÓN CLÍNICA

Corea; Discinesia; Discinesia (Inicio juvenil); Disquinesia paroxística; Disquinesia paroxística (Inicio juvenil); Distonía; Distonía de extremidades; Distonía de pierna; Distonía del brazo; Inicio juvenil.
(Información clínica reportada atendiendo a la nomenclatura HPO.)

Edad de manifestación: 10 año(s).

Historia familiar: Desconocido.

Hermanos no afectados.

Padres consanguíneos: No.



RESULTADO NEGATIVO

INTERPRETACIÓN

No se identificó ninguna variante, incluyendo variantes en el número de copias, clínicamente relevante para el fenotipo descrito.

RECOMENDACIONES

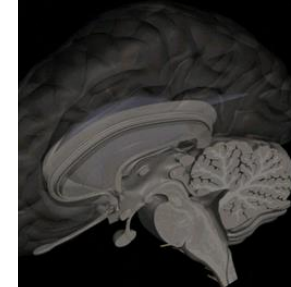
- Se recomienda proceder a la secuenciación del genoma completo que tiene una tasa de clarificación adicional del 15-18% en comparación con la secuenciación del exoma completo.
- Se recomienda asesoramiento genético.

ALTERACIONES GENÉTICAS ESTUDIO POR SECUENCIACIÓN COMPLETA DEL EXOMA



GEN	COORDENADAS DE LA VARIANTE	CAMBIO DE AMINOÁCIDO	IDENTIFICADOR SNP	CIGOSIDAD	PARÁMETROS IN SILICO*	FRECUENCIAS ALÉLICAS**	TIPO Y CLASIFICACIÓN***
CFTR	NM_000492.3:c.350G>A	p.(Arg117His)	rs78655421	heterocigota	PolyPhen: Probablemente deletérea Align-GVGD: C15 SIFT: Deletérea MutationTaster: Patogénica Conservación_nt: alta Conservación_aa: alta	gnomAD: 0.0014 ESP: 0.0015 1000 G: 0.00023 CentoMD: 0.00083	Cambio de sentido Patogénica (clase 1)

Anotación de la variante en base a OTFA (utilizando VEP v94). * AlignGVD: C0: menor probabilidad de interferir con la función, C65: mayor probabilidad de interferir con la función; predictores de splicing: Ada y RF scores. ** Genome Aggregation Database (gnomAD), Exome Sequencing Project (ESP), 1000Genomes Project (1000G) y CentoMD® (última versión)



Dr. Patricio Guerra
Clínica Universitaria Puerto Montt
Neurology
Av. Bellavista No 123
5480000 Puerto Montt
Chile

N° pedido: 63138972

Fecha de recepción: 04 sep. 2023

Tipo de Muestra / Día de toma de muestra:

sangre, CentoCard® / 26 jul. 2023

Fecha del reporte: 18 sep. 2023

Tipo de reporte: Reporte final



N° paciente: **1830367**, Nombre: **Marcelo-Ignacio**, Apellido: **Villarroel-Rogel**
F. nacimiento: **07 jun. 1999**, Sexo: **masculino**, Ref. externa: **20.233.231-5**

Destinatarios adicionales: Dr. Patricio Guerra, Clínica Universitaria Puerto Montt, Neurology, Av. Bellavista No 123, 5480000 Puerto Montt, Chile; Mrs. Claudia Diaz Sanhueza, Servicios geneticos y asociados SpA, Genetica, La Concepcion 7633, La Florida, 8150215 Santiago, Chile.

Prueba solicitada: CentoGenome® Solo Reanalysis

INFORMACIÓN CLÍNICA

Accidente cerebrovascular; Ausencia del lenguaje; Autismo; Bermellón del labio superior fino; Cara triangular; Catarata; Ceja gruesa; Comportamiento autista; Convulsiones; Dedos de la mano largos; Desarrollo insuficiente del hélix; Discapacidad intelectual severa; Espasmos epilépticos; Hélix grueso; Litiasis renal; Macrotia; Nariz prominente; Ojos hundidos; Oreja de forma redonda; Puente nasal prominente; Retardo global del desarrollo; Sinofridia.

(Información clínica reportada atendiendo a la nomenclatura HPO)

Pruebas realizadas anteriormente en CENTOGENE con resultados negativos: CentoGenome Solo (N° pedido: 63129982).

Historia familiar: Sí.

Primo materno: Comportamiento autista, Retardo global del desarrollo, Retraso en el desarrollo del habla y el lenguaje; Hermanos no afectados.

Padres consanguíneos: No.



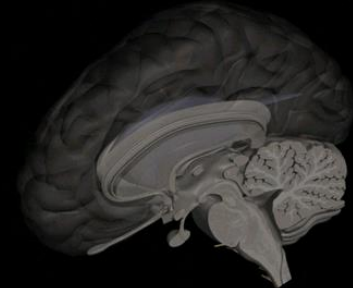
RESULTADO NEGATIVO

INTERPRETACIÓN

No se detectaron variantes clínicamente relevantes para el fenotipo descrito.

RECOMENDACIONES

- Recomendamos la reevaluación de los datos de secuenciación cada 12 meses o si hay cambios fenotípicos.
- Se recomienda asesoramiento genético.



1. Precios:

Epidasd Panel: incluye todos los genes relevantes para el diagnostico de Epilepsia, Discapacidad intelectual y transtorno del espectro autista (1740 genes)

Precio sin envío: \$600.00

Precio con envío incluido: \$650.00

Precio especial por envío de 3 muestras al mismo tiempo: \$600.00 (envío GRATIS)

EpidasdACT Panel: incluye todos lo genes accionables para los cuales existe un tratamiento definido en medicina de precision (200 genes)

Precio sin envío: \$500.00

Precio con envío: \$550.00


Precio Especial por envío de 3 muestras al mismo tiempo: \$500.00 (envío GRATIS)

Exoma:

Precio sin envío: \$600.00

Precio con envío incluido: \$650.00

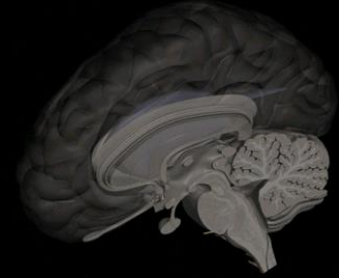
Precio especial por envío de 3 muestras al mismo tiempo: \$600.00 (envío GRATIS)

PRESTACIONES	CÓDIGO FONASA 	CÓDIGO INTERNO	HÁBIL INHÁBIL (% RECARGO)	VALOR PARTICULAR	VALOR FONASA	VALOR ISAPRE	GLOSA FONASA
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Tipo de prestación: RESONANCIA NUC.MAGNETICA

Horario hábil: Lunes a Viernes de 08.00 a 21.00 horas y sábados de 08.00 a 14.00 horas (con excepción de los días festivos)

RNM COLUMNA CERVICAL	0405005	583260	Hábil	\$916.191	\$203.070	\$916.191
			Inhábil (recargo 50%)	\$1.374.287	\$203.070	\$1.374.287
RNM COLUMNA DORSAL	0405006	583261	Hábil	\$916.191	\$211.190	\$916.191
			Inhábil (recargo 50%)	\$1.374.287	\$211.190	\$1.374.287
RNM COLUMNA LUMBAR	0405007	583262	Hábil	\$748.183	\$203.070	\$748.183
			Inhábil (recargo 50%)	\$1.122.275	\$203.070	\$1.122.275
RNM CRÁNEO - CEREBRO U OIDOS, BILATERAL	0405001	583001	Hábil	\$916.191	\$203.070	\$916.191
			Inhábil (recargo 50%)	\$1.374.287	\$203.070	\$1.374.287



Farmacogenética

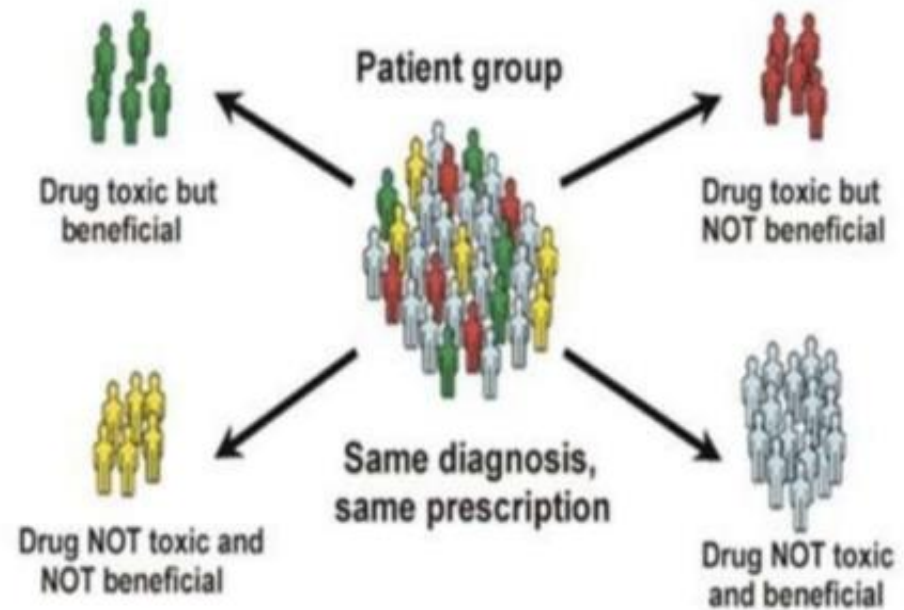
(término introducido en 1947, A Motulsky)

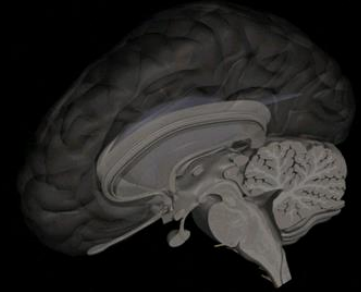
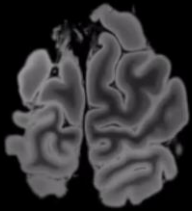
Estudio del rol de la
variación genética
heredada y adquirida en
la respuesta a fármacos

Uso de tests
genéticos/genómicos que
proveen información
para:

Selección de agentes
terapéuticos

Selección de dosis de
agentes terapéuticos





NEUROPEDIATRÍA

Revisión tópicos de interés en Neurodesarrollo para el Pediatra

Sociedad Chilena de Pediatría Filial Los Lagos

DR. PATRICIO GUERRA

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