ESCUELA DE OSTEOPATIA DE MADRID

CONOCIMENTO:

PROPOSICIONAL O TEÓRICO:

“ SABER QUE”.

PROCEDIMENTAL O PRÁCTICO:

“ SABER CÓMO”

CORE O NUCLEO: SACAR FACTOR COMÚN Y SIMPLIFICAR LA REALIDAD.

1.- Introducción a la organización del sistema endocrino.

1. ***Importancia de la endocrinología .***
2. ***Hormonas : tipos de secreción.***
3. ***Funciones hormonales.***
4. ***Coordinación neuroendocrina. Dos sistemas , diferente velocidad.***
5. ***PRINCIPALES GLÁNDULAS ENDOCRINAS- ESTRUCTUR QUÍMICA.***
6. ***Transporte , metabolismo y degradación.***
7. ***Características comunes y diferencias entre las hormonas peptídicas y esteroideas.***
8. ***Ritmos Circadianos. Cuándo es ideal tratar o ejercitar.***

Importancia de la endocrinología

ENDOCRINOLOGÍA

"La Endocrinología es la ciencia dedicada al estudio de las hormonas y sus glándulas de producción.

Estudia los efectos normales de sus secreciones, y los trastornos derivados del mal funcionamiento de las mismas"。

1.- Introducción a la organización del sistema endocrino.

1.1.-Importancia de la endocrinología .

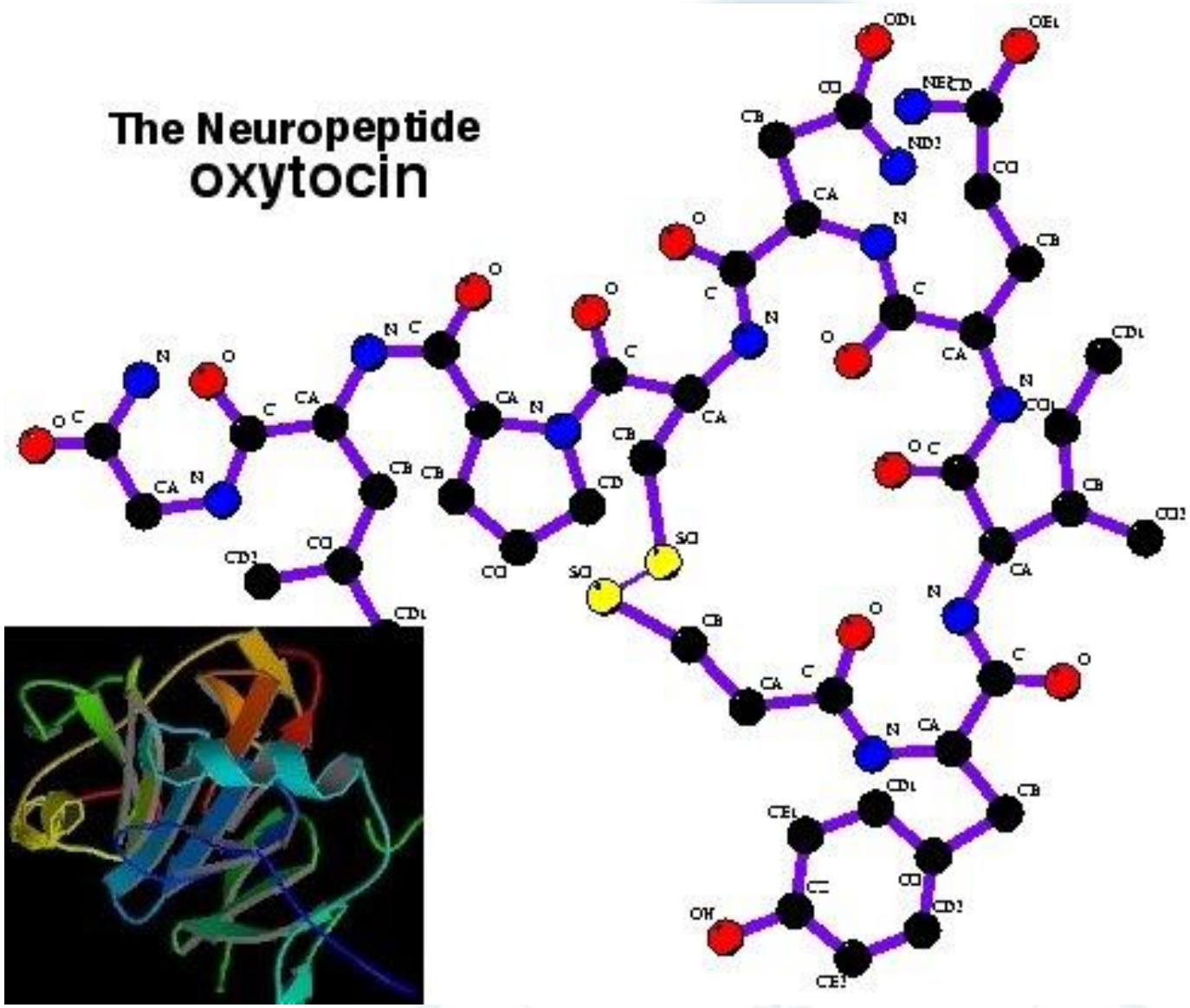
1.2.-Hormonas : tipos de secreción.

1.3.-Funciones hormonales.

1.4.-Coordinación neuroendocrina. Dos sistemas , diferente velocidad.

1.1.-IMPORTANCIA DE LA ENDOCRINOLOGÍA:

- ***¿ Qué es una hormona ? Es un compuesto químico que es secretado a la circulación por glándulas o células endocrinas , que es capaz de unirse a receptores específicos en la membrana celular de órganos diana y que genera una determinada respuesta.***



Los desórdenes endocrinos ocurren de una de estas dos maneras

POR DEFECTO:

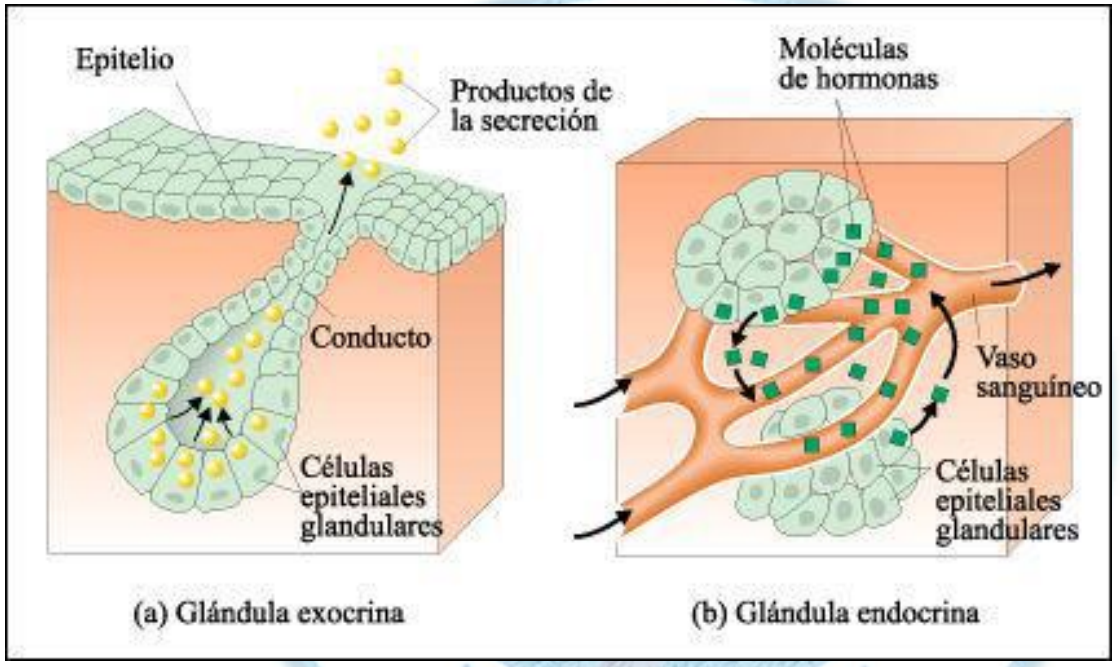
Tejido endocrino anormal:1.- por insuficiencia de los componentes necesarios para la síntesis ej. yodo para la tiroxina
2.-por la destrucción de células por anticuerpos autoinmunes ej. insuficiencia suprarrenal idiopática.
3.-Sensibilidad anormal del tejido a su órgano DIANA

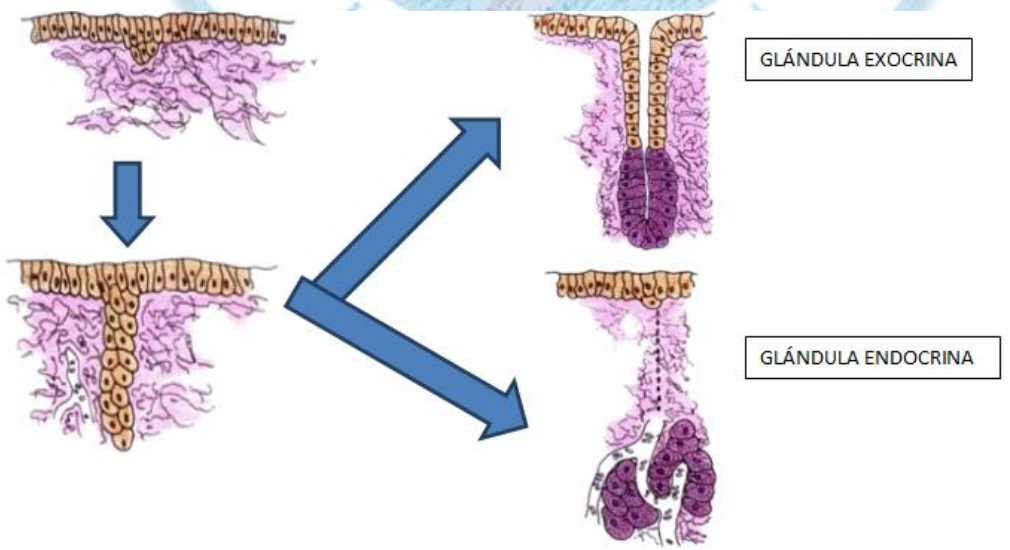
POR EXCESO:Las hormonas pueden secretarse inversamente en exceso cuando un tumor se desarrolla ej. el ferrocromocitoma, que es un tumor raro de la médula suprarrenal

ENDOCRINOLOGÍA:

Las ***glándulas endocrinas*** son glándulas de secreción interna ya que vierten sus secreciones directamente a la sangre.

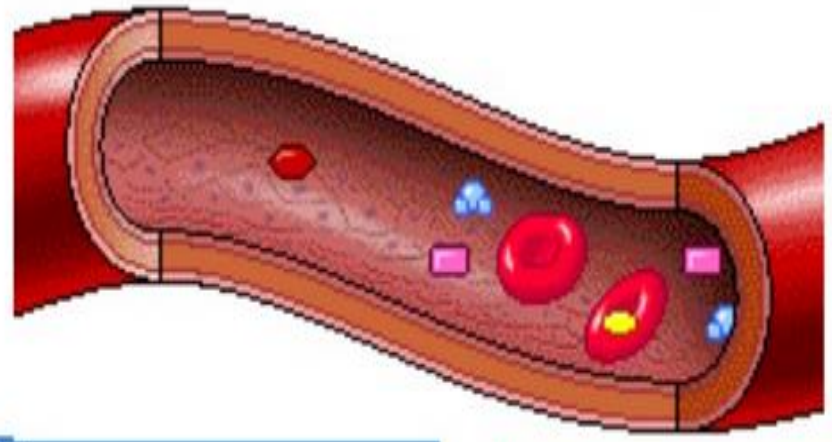
Las ***glándulas exocrinas*** (sebáceas y sudoríparas …)vierten al exterior sus secreciones.





¿ Cómo podemos mejorar nosotros el transporte, los efectos y la semivida de la hormona?

- Transporte :regulación del equilibrio ácido base y de la osmolalidad → nutrición+ TRATAMIENTO DEL HÍGADO INTESTINO Y RIÑON..
- Podemos , si conocemos las sinergias y los efectos permisivos : TRATAMIENTO SISTEMA FASCIAL, TRATAMIENTO SNV, TRABAJO SOBRE LA PIEL COMO ÓRGANO ENDOCRINO(SE EXPLICA MÁS ADELANTE).
- Para regular la semivida es fundamental conocer las enzimas implicadas y conocer la IMPORTANCIA DEL TRABAJO OSTEOPÁTICO DEL HÍGADO .



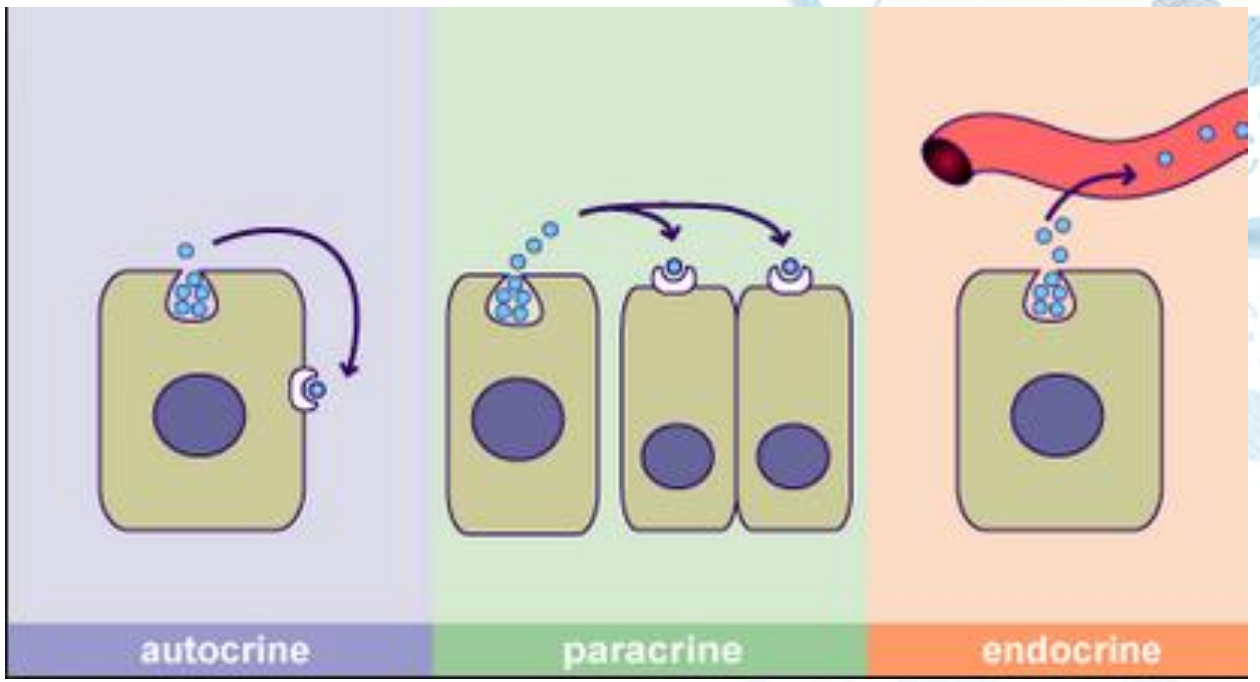
Nota:
Cuando en la sangre hay una cantidad anormal a la necesitada, la glándula recibe la orden de inhibir o frenar la producción de esa hormona

Mecanismo de Eliminación

BILIS Y ORINA

2.-Hormonas: tipos de secreción.

a)Autocrina: sobre la actividad de la propia célula secretora.
b)Paracrina: provoca respuestas locales sobre células vecinas (islotes de langerhans).
c)Endocrina: la sustancia es liberada en el torrente sanguíneo y afecta a órganos distantes dentro del cuerpo
d)Neurocrina: hormonas liberadas por neuronas al torrente circulatorio que actúan sobre células distantes



El sistema endocrino está caracterizado por la presencia de glándulas que segregan sustancias/hormonas a la sangre y que actúan a distancia, es decir, de manera **endocrina- holocrina.**

1. PINEAL + Hipófisis o pituitaria
2. Tiroides
3. Paratiroides
4. Glándulas adrenales
5. Páncreas
6. Ovario y testículos

El sistema endocrino interviene en múltiples funciones metabólicas implicándose en:

1. **Reproducción** (ejemplos: LH, FSH, testosterona). Se dan cuadros de mala diferenciación sexual.
2. **Crecimiento y desarrollo** (ejemplos: GH) . Se dan cuadros de falta de crecimiento.
3. **Maduración de los glóbulos rojos:** Eritropoyetina (segregada en el riñón). Se dan cuadros de no maduración de GR.
4. **Homeostasis** (ejemplos: hormonas tiroideas, cortisol, PTH).
5. **Metabolismo.** Se dan cuadros de alteración del metabolismo de las glándulas suprarrenales.

ESQUEMAS RESUMEN:

Conceptos básicos:

Endocrinología – hormonas y gl.endocrinas(mal funcionamiento)

Sistema Endocrino: conjunto de glándulas , tejidos , células

Hormonas: compuestos químicos – respuesta autocrina, paracrina, endocrina, neurocrina. Diferentes funciones.+ SNC→ PAPEL CENTRAL EN RESPUESTAS.

Glándulas: Hipotálamo:+ GHRH,CRH,TRH,GnRH, GHIH,PIH,ADH, Oxitocina.

Hipófisis: GH,TSH,ACTH,FSH,LH,MSH,ADH,oxitocina.

Tiroides: T3-T4, CALCITONINA.

Paratiroides: PTH

Adrenales: adrenalina, noradrenalina, dopamina, cortisol, aldosterona, andrógenos.

Páncreas: insulina, glucagón, somatostatina.

Testículo: testosterona.

Ovarios: Estrógenos, Progesterona.

Transporte

Hormonas hidrosolubles

Catecolaminas y hormonas polipeptídicas
Libres en palsma o unidas a prot. plasmáticas

Hormonas liposolubles

Tiroideas y esteroideas
Unidas a prot. plasmáticas
- Inespecíficas: albúmina
- Específicas: TBG, etc...

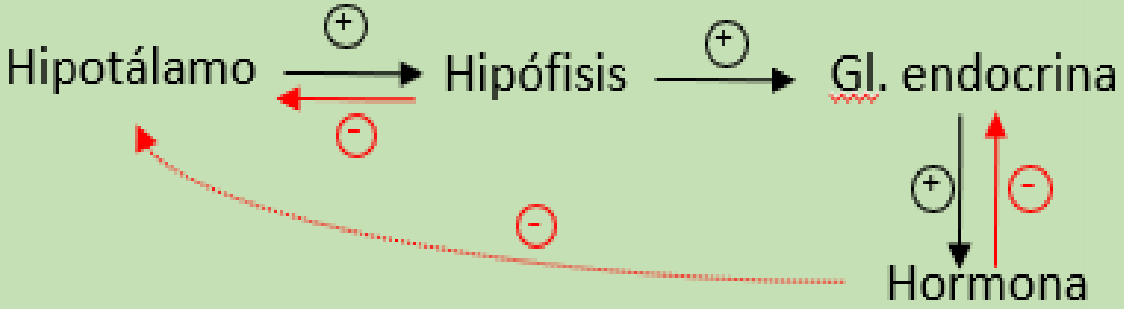
Libres → efecto y degradadas

Unidas → vida media mayor

Regulación hormonal

Control feed-back negativo

Control hipotálamo-hipofisario

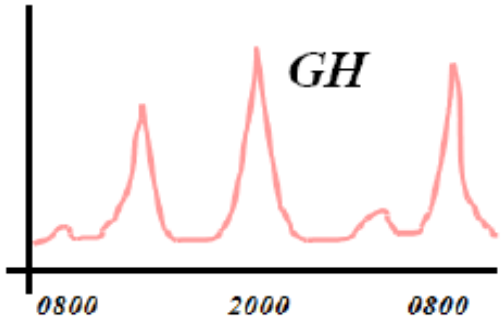


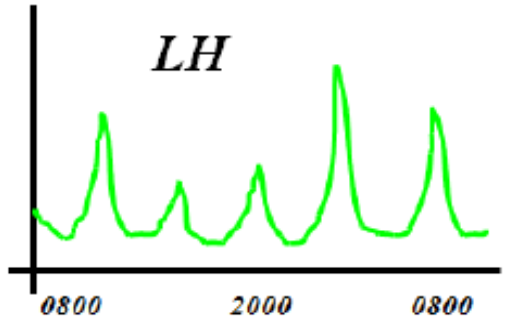
Control cronotrópico

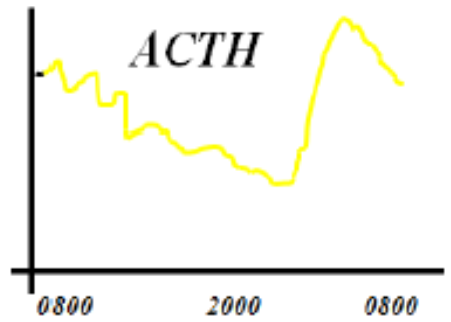
Secreción pulsátil
Ritmos circadianos ACTH, cortisol)
Sueño (GH)
Ciclo lunares (gonadotropinas)

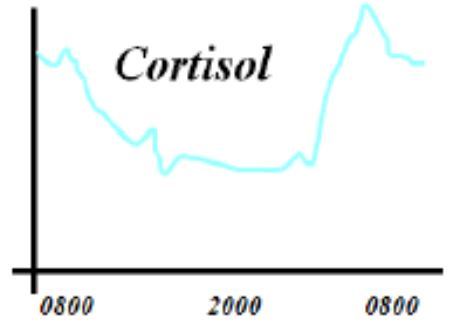
Otros

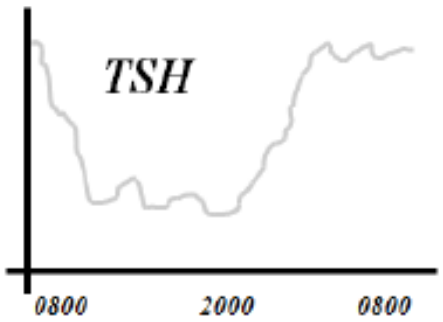
Edad, estrés, dieta, ejercicio, cambios medio interno....











CLASIFICACION DE LAS HORMONAS POR SU NATURALEZA QUIMICA

AMINAS

Derivados de triptófano y tirosina

ejemplos

- melatonina
- calcitonina
- serotonina
- Tiroxina T3 y TriyodotironinaT4

POLIPEPTIDOS Y PROTEINAS

Poli péptidos grandes de mas de 100 aminoácidos

ejemplos

- Glucagon
- H. anti diurética
- insulina
- H. Del crecimiento

GLUCOPROTEINAS

Proteína unida a un carbohidrato

ejemplos

- Folículo estimulante
- H. luteinizante
- Tirotropina (TSH)

ESTEROIDES

Derivan del colesterol

ejemplos

- Testosterona
- estradiol
- progesterona
- cortisol
- aldosterona

Estructura química

Derivadas de aas.

Tiroideas y adrenalina
A prtir de Tyr. Los dipéptidos y aa se dan por vía oral

Hormonas peptídicas/proteicas

ADH y oxitocina/ insulina y glucagón. Vía parenteral 54 aa.
Prehormona – péptido señal (se pierde en RER)
Se liberan por exocitosis

Esteroideas

Sexuales, cortisol, aldosterona
Derivadas de colesterol, se pueden dar vía oral.

Eicosanoides (derivan del ácido araquidónico)

Leucotrienos, prostaglandinas, tromboxanos

Metabolismo y eliminación:

Degradación:

Proteolisis.

Oxidación, hidroxilación y conjugación.

En tejidos diana e hígado. Productos metabólicos eliminados vía biliar o renal.

Pequeña fracción hormonal se elimina sin cambio.

Mecanismos de acción hormonal

Tejido con receptores (llave-cerradura) de membrana o intracelulares

Hormonas peptídicas, catecolaminas y eicosani¡oides

Unión H-R activa 2º mensajeros ⟶ cambios
- En act. Enzimática
- En permeabilidad membrana
- Secreción hormonal por exocitosis
- En la concentración enzimas o prot. intracelulares

Esteroides, vit. D3 y T3

Atraviesan membrana, se unen a receptores citoplasmáticos y activan o inhiben síntesis de proteína
Respuesta más tardía pero más duradera

Características comunes

Down-regulation:si hay excesiva estimulación
Up-regulation: *respuesta excesiva a pesar de concentración baja*

Factores que influyen en la acción hormonal:

Concentración hormona, nº receptores, vida media, efectos otras sustancias (agonista/ antagonista, sinergismo, acción permisiva)

Conceptos básicos

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Diferentes funciones
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- GHIH, PIH, ADH, oxitocina
Hipófisis: GH, TSH, ACTH, FSH, LH, MSH, ADH, oxitocina
Tiroides: T3, T4, calcitonina
Paratiroides:PTH
Adrenales: Adrenalina, noradrenalina, dopamina
cortisol, aldosterona, andrógenos, corticoadrenales
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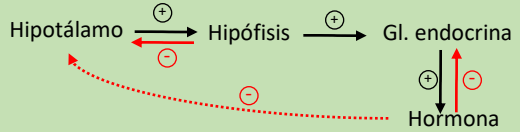

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Degradación

Proteolisis
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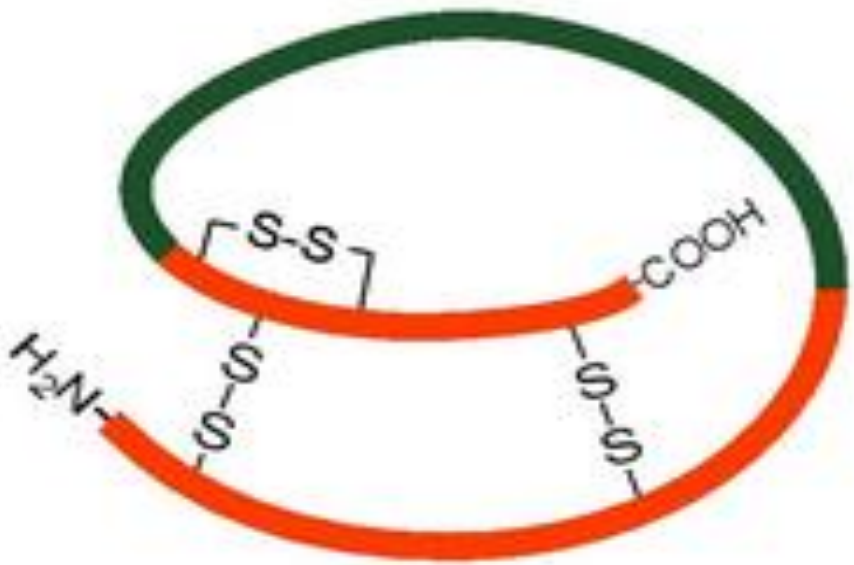
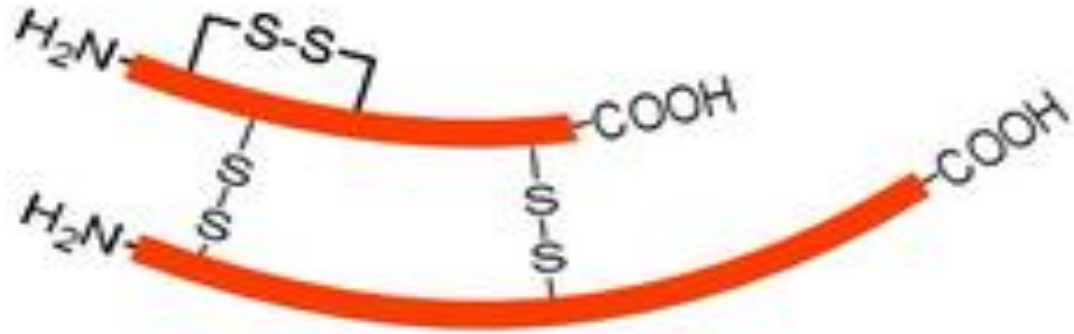


Proinsulina

Péptido C

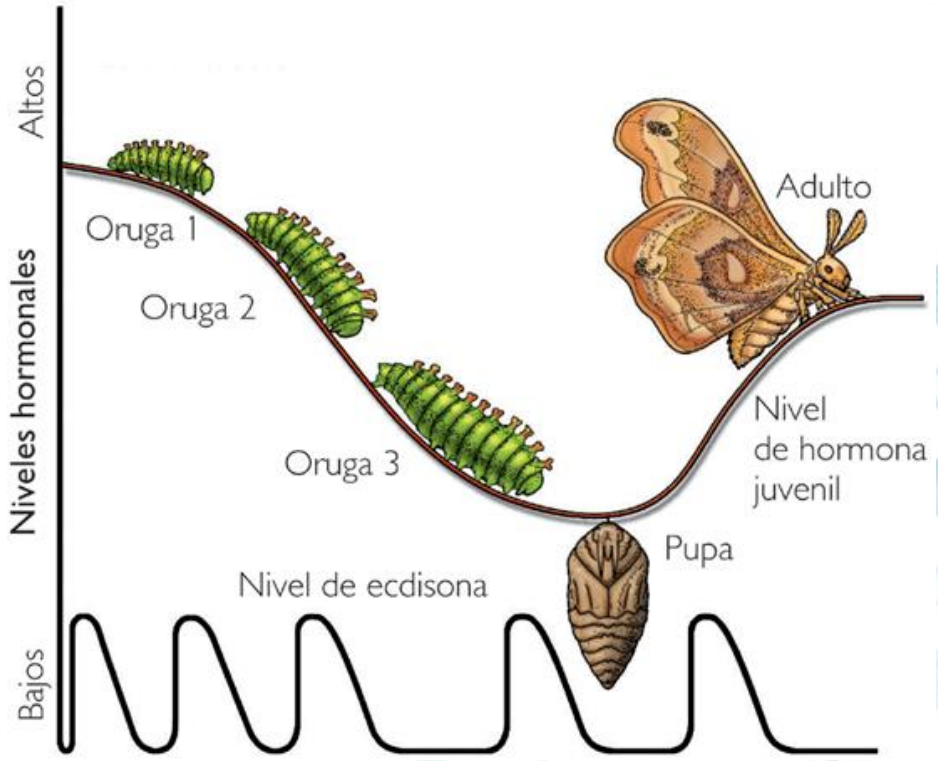


Insulina

3.- FUNCIONES HORMONALES:

3.-¿ qué funciones controlan las hormonas?

- Emoción y sistema inmunológico.
- Composición corporal.
- Procesos digestivos.
- Peso corporal.
- Conducta alimentaria.
- Reproducción y características sexuales.
- Volemia, presión, osmolalidad y pH sanguíneo.
- Metabolismo.
- Termorregulación.



4.- INTEGRACIÓN NEUROENDOCRINA:

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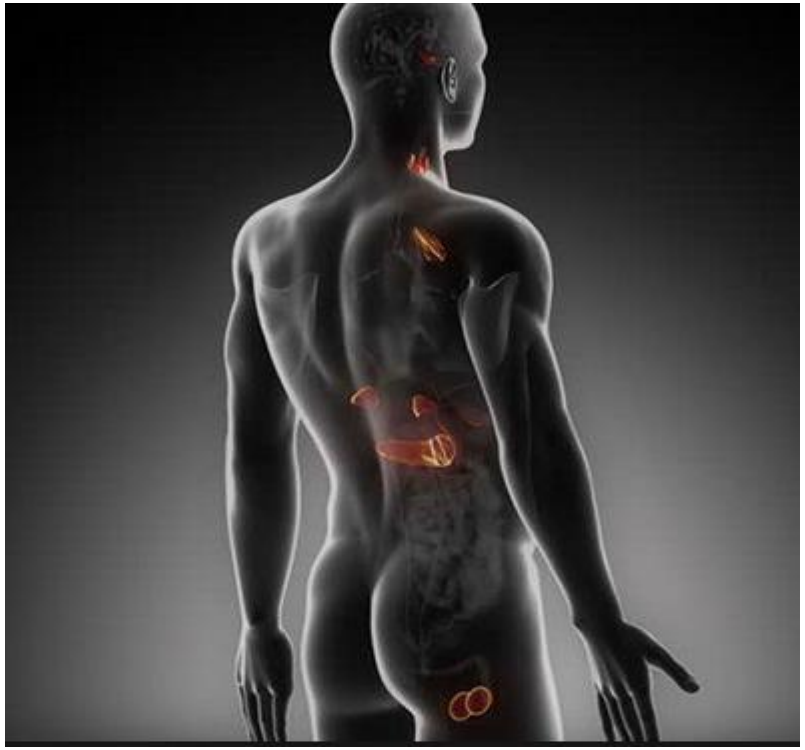
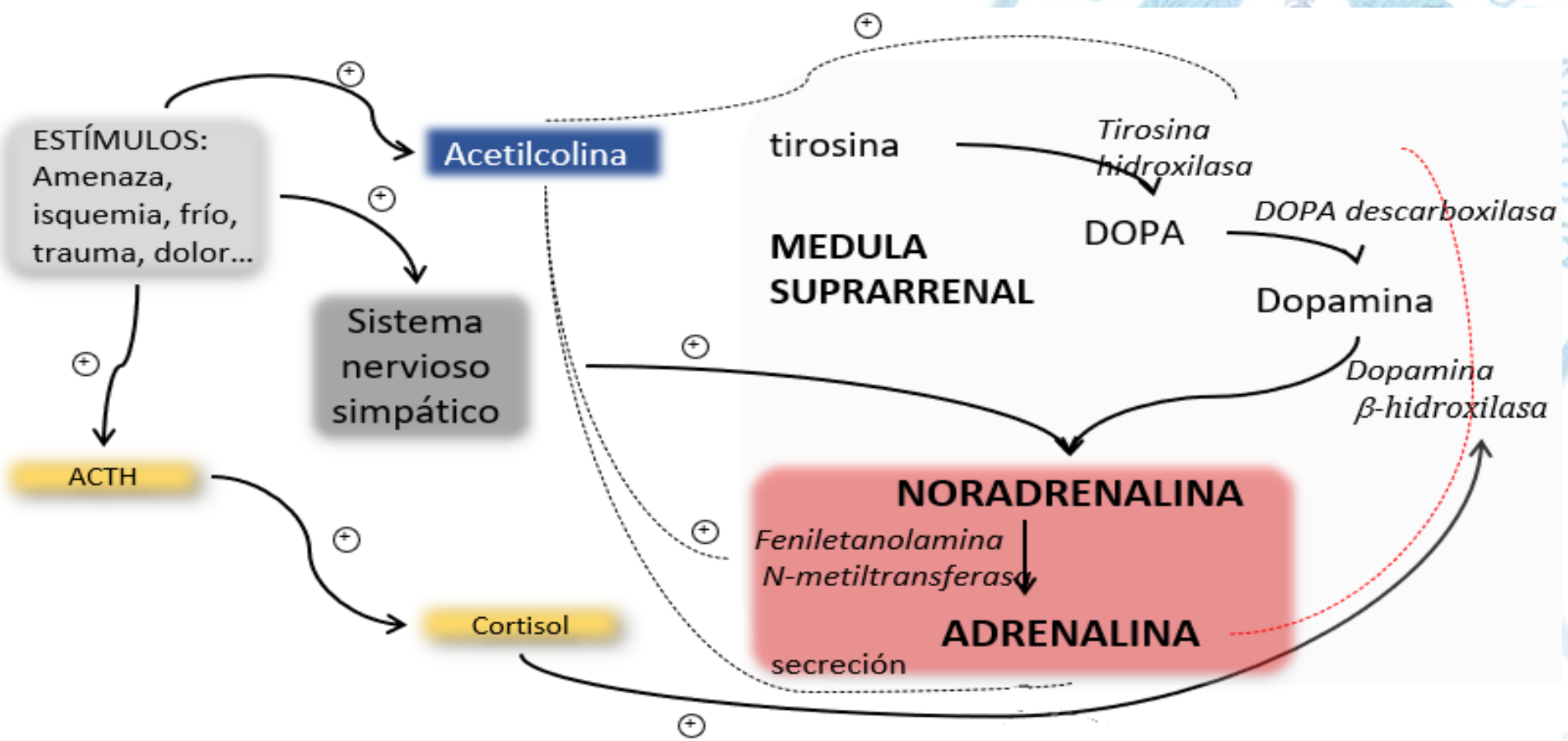
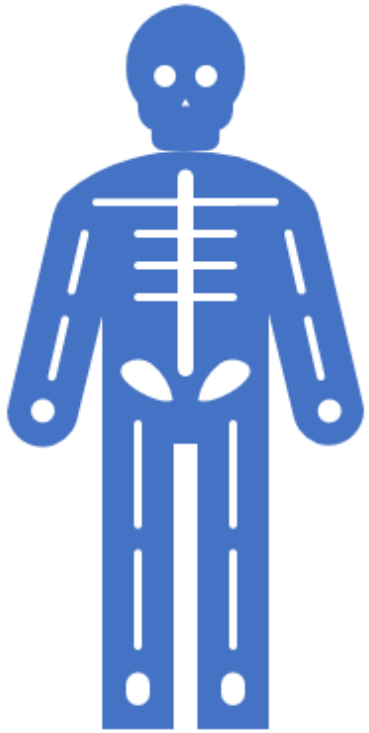


- El **sistema nervioso** implica la comunicación a través de neurotransmisores, su acción es rápida(milisegundos) y su duración es breve.
- El **sistema endocrino** implica hormonas, es lento en regularse (minutos a horas) y su duración es larga.

¿CÓMO SE INTERRELACIONAN EL SISTEMA ENDOCRINO Y EL SNV?





- Las **vías eferentes de los nervios somáticos** constan de una sola neurona y liberan **acetilcolina sobre receptor nicotínico.** La sinapsis neuromuscular y ganglionar es rápida , un milisegundo .
- Las **fibras simpáticas preganglionares** liberan **acetilcolina sobre receptor nicotínico** y las **postganglionares noradrenalina sobre receptores alfa o beta adrenérgicos**. Sinapsis lentas 2-3ms (ms liso, glándulas , corazón)**excepción: glándulas sudoríparas acetilcolina sobre receptor muscarínico.**
- Las **fibras parasimpáticas preganglionares liberan acetilcolina sobre receptor nicotínico y las postganglionares acetilcolina sobre receptor muscarínico**.

DIFERENCIA TIEMPO EFECTO SNSIMPATICO Y PARASIMPÁTICO

El ciclo del mediador colinérgico implica una rápida hidrólisis por la acetilcolinesterasa.

Frente al parasimpático , las neuronas adrenérgicas periféricas son neuronas postganglionares cuyos cuerpos celulares están situados en el ganglio simpático.

Presentan largos axones que terminan en una serie de varicosidades con grandes y granuladas vesículas que sintetizan y liberan noradrenalina.

La liberación es por exocitosis como el colinérgico CON LA DIFERENCIA DE QUE UNA NEURONA ADRENÉRGICA CONTIENE INFINIDAD DE VARICOSIDADES DE FORMA QUE UN IMPULSO NERVIOSO GENERA LIBERACIÓN DE VESÍCULAS EN UN AMPLIA ÁREA MIENTRAS QUE EL COLINÉRGICO SE LIBERA EN UNA ZONA REDUCIDA.

LA NORADRENALINA SE DEGRADA LENTAMENTE POR MAO Y CATECOLMETILTRANSFREASA.

El tratamiento osteopático :

Plaza-Manzano G, Molina-Ortega F, Lomas-Vega R, Martinez-Amat A, Achalandabaso A, Hita-Contreras F. Changes in biochemical markers of pain perception and stress response after spinal manipulation. J Orthop Sports Phys Ther. 2014 Apr;44(4):231–9.

La presión arterial.

Win NN, Jorgensen AMS, Chen YS, Haneline MT. Effects of Upper and Lower Cervical Spinal Manipulative Therapy on Blood Pressure and Heart Rate Variability in Volunteers and Patients With Neck Pain: A Randomized Controlled, Cross-Over, Preliminary Study. J Chiropr Med. 2015 Mar;14(1):1–9.

J Orthop Sports Phys Ther. 2014 Apr;44(4):231-9. doi: 10.2519/jospt.2014.4996. Epub 2014 Jan 22.

Changes in biochemical markers of pain perception and stress response after spinal manipulation.

Plaza-Manzano G[1], Molina-Ortega F, Lomas-Vega R, Martínez-Amat A, Achalandabaso A, Hita-Contreras F.

Author information

INCREMENTO DE NEUROTENSINA , OXITOCINA Y CORTISOL

Abstract

STUDY DESIGN: Controlled, repeated-measures, single-blind randomized study.

OBJECTIVES: To determine the effect of cervical or thoracic manipulation on neurotensin, oxytocin, orexin A, and cortisol levels.

BACKGROUND: Previous studies have researched the effect of spinal manipulation on pain modulation and/or range of movement. However, there is little knowledge of the biochemical process that supports the antinociceptive effect of spinal manipulation.

METHODS: Thirty asymptomatic subjects were randomly divided into 3 groups: cervical manipulation (n = 10), thoracic manipulation (n = 10), and nonmanipulation (control) (n = 10). Blood samples were extracted before, immediately after, and 2 hours after each intervention. Neurotensin, oxytocin, and orexin A were determined in plasma using enzyme-linked immuno assay. Cortisol was measured by microparticulate enzyme immuno assay in serum samples.

RESULTS: Immediately after the intervention, significantly higher values of neurotensin (P<.05) and oxytocin (P<.001) levels were observed with both cervical and thoracic manipulation, whereas cortisol concentration was increased only in the cervical manipulation group (P<.05). No changes were detected for orexin A levels. Two hours after the intervention, no significant differences were observed in between-group analysis.

CONCLUSION: The mechanical stimulus provided by spinal manipulation triggers an increase in neurotensin, oxytocin, and cortisol blood levels. Data suggest that the initial capability of the tissues to tolerate mechanical deformation affects the capacity of these tissues to produce an induction of neuropeptide expression. J

PMID: 24450367 DOI: 10.2519/jospt.2014.4996

J Chiropr Med. 2015 Mar;14(1):1-9. doi: 10.1016/j.jcm.2014.12.005. Epub 2015 Feb 7.

Effects of Upper and Lower Cervical Spinal Manipulative Therapy on Blood Pressure and Heart Rate Variability in Volunteers and Patients With Neck Pain: A Randomized Controlled, Cross-Over, Preliminary Study.

Win NN[1], Jorgensen AM[1], Chen YS[2], Haneline MT[3].

Author information

LA MANIPULACIÓN CERVICAL PROMUEVE DOMINANCIA DEL PARASIMPÁTICO EN PACIENTES CON CERVICALGIA.

Abstract

OBJECTIVE: The aims of this study were to examine autonomic nervous system responses by using heart rate variability analysis (HRV), hemodynamic parameters and numeric pain scale (NPS) when either upper (C1 and C2) or lower (C6 and C7) cervical segments were manipulated in volunteers, and whether such response would be altered in acute mechanical neck pain patients after spinal manipulative therapy (SMT).

METHODS: A randomized controlled, cross-over, preliminary study was conducted on 10 asymptomatic normotensive volunteers and 10 normotensive patients complaining of acute neck pain. HRV, blood pressure (BP) and heart rate (HR), and NPS were recorded after upper cervical and lower cervical segments SMT in volunteer and patient groups.

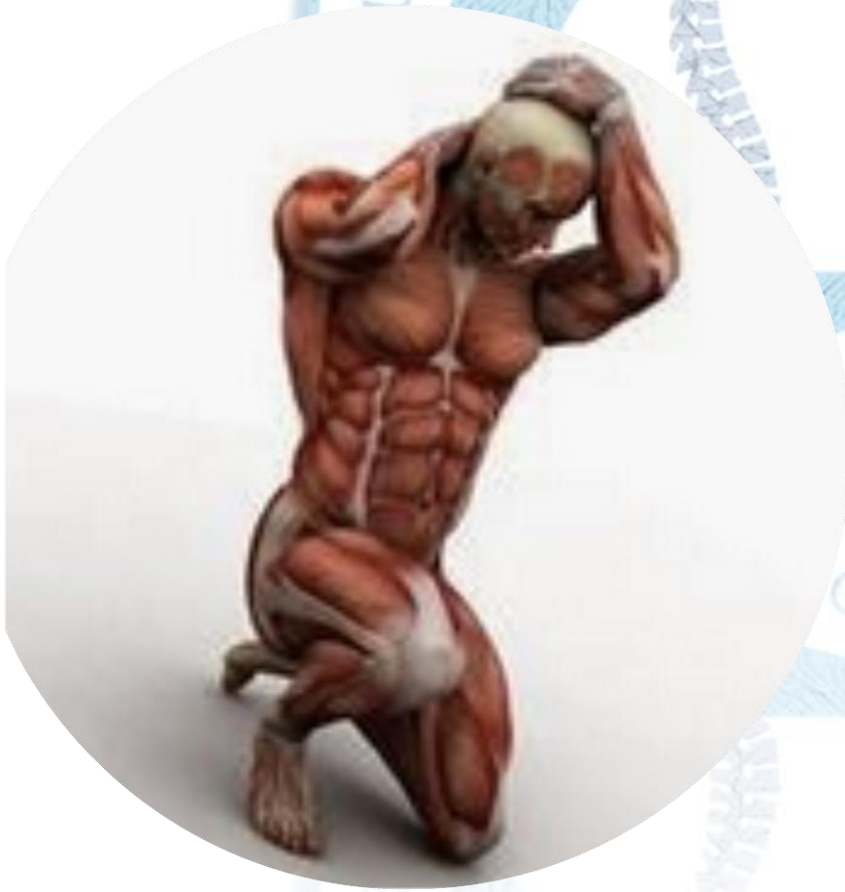
RESULTS: The standard deviation of average normal to normal R-R intervals (SDNN) increased (83.54 ± 22 vs. 105.41 ± 20; P = .02) after upper cervical SMT. The normalized unit of high frequency (nuHF), which shows parasympathetic activity, was predominant (40.18 ± 9 vs. 46.08 ± 14) after upper cervical SMT (P = .03) with a significant decrease (109 ± 10 vs. 98 ± 5) in systolic BP (P = .002). Low frequency to high frequency (LF/HF) ratio, which shows predominance of sympathetic activity increased (1.05 ± 0.7 vs. 1.51 ± 0.5; P = .02) after lower cervical SMT in the healthy volunteers group. However, there was an increase in SDNN (70.48 ± 18 vs. 90.23 ± 20; P = .02 and 75.19 ± 16 vs 97.52 ± 22; P = .01), a decrease in LF/HF ratio (1.33 ± 0.3 vs. 0.81 ± 0.2; P = .001 and 1.22 ± 0.4 vs. 0.86 ± 0.3; P = .02), which was associated with decreased systolic BP (105 ± 10 vs. 95 ± 9; P = .01 and 102 ± 9 vs. 91 ± 10; P = .02) and NPS scores (3 ± 1 vs. 0; P = .01 and 3 ± 1 vs. 1 ± 1; P = .03) following both upper and lower cervical SMT in the patient's group. The baseline HR was 67 ± 9 vs 64 ± 5 (upper cervical) and 65 ± 7 vs 69 ± 11 (lower cervical) in both the healthy volunteer' and patient' groups.

CONCLUSION: Upper cervical SMT enhances dominance of parasympathetic and lower cervical SMT enhances dominance of sympathetic activity in this young volunteer group. However, dominance of parasympathetic activity was found in patients with neck pain that received both upper and lower cervical SMT.

KEYWORDS: Blood pressure; Heart rate; Manipulation; Spinal

Kolberg C, Horst A, Moraes MS, Duarte FCK, Riffel APK, Scheid T, et al. Peripheral oxidative stress blood markers in patients with chronic back or neck pain treated with high-velocity, low-amplitude manipulation. J Manipulative Physiol Ther. 2015 Feb;38(2):119–29.

Inami A, Ogura T, Watanuki S, Masud MM, Shibuya K, Miyake M, et al. Glucose Metabolic Changes in the Brain and Muscles of Patients with Nonspecific Neck Pain Treated by Spinal Manipulation Therapy: A [(18)F]FDG PET Study. Evid Based Complement Alternat Med. 2017;2017:4345703.



Atendiendo a esta explicación fisiológica :

- Sampath et al (2017) demostraron que la manipulación involucra al sistema nervioso simpático y al sistema endocrino.
- Mc Partland et al (2005) demostraron que la manipulación altera los cannabinoides endógenos producidos en la sustancia gris periacueductual.
- Plaza y Manzano (2014)demostraron que la manipulación incrementa los niveles de cortisol , IL -1 , IL-8 , NEUROTENSINA Y OXITOCINA.

TOMADO DE F. RICARD: Mecanismo de acción biológico de las manipulaciones vertebrales con HVT.

Musculoskelet Sci Pract. 2017 Jun;29:120-131. doi: 10.1016/j.msksp.2017.04.004. Epub 2017 Apr 5.

Changes in biochemical markers following spinal manipulation-a systematic review and meta-analysis.

LA MANIPULACIÓN ESPINAL INCREMENTA SUSTANCIA P , INTERLEUKINAS, OXITOCINA , NEUROTENSINA E INFLUENCIA LOS NIVELES DE CORTISOL.

Kovanur-Sampath K[1], Mani R[2], Cotter J[3], Gisselman AS[2], Tumilty S[2].

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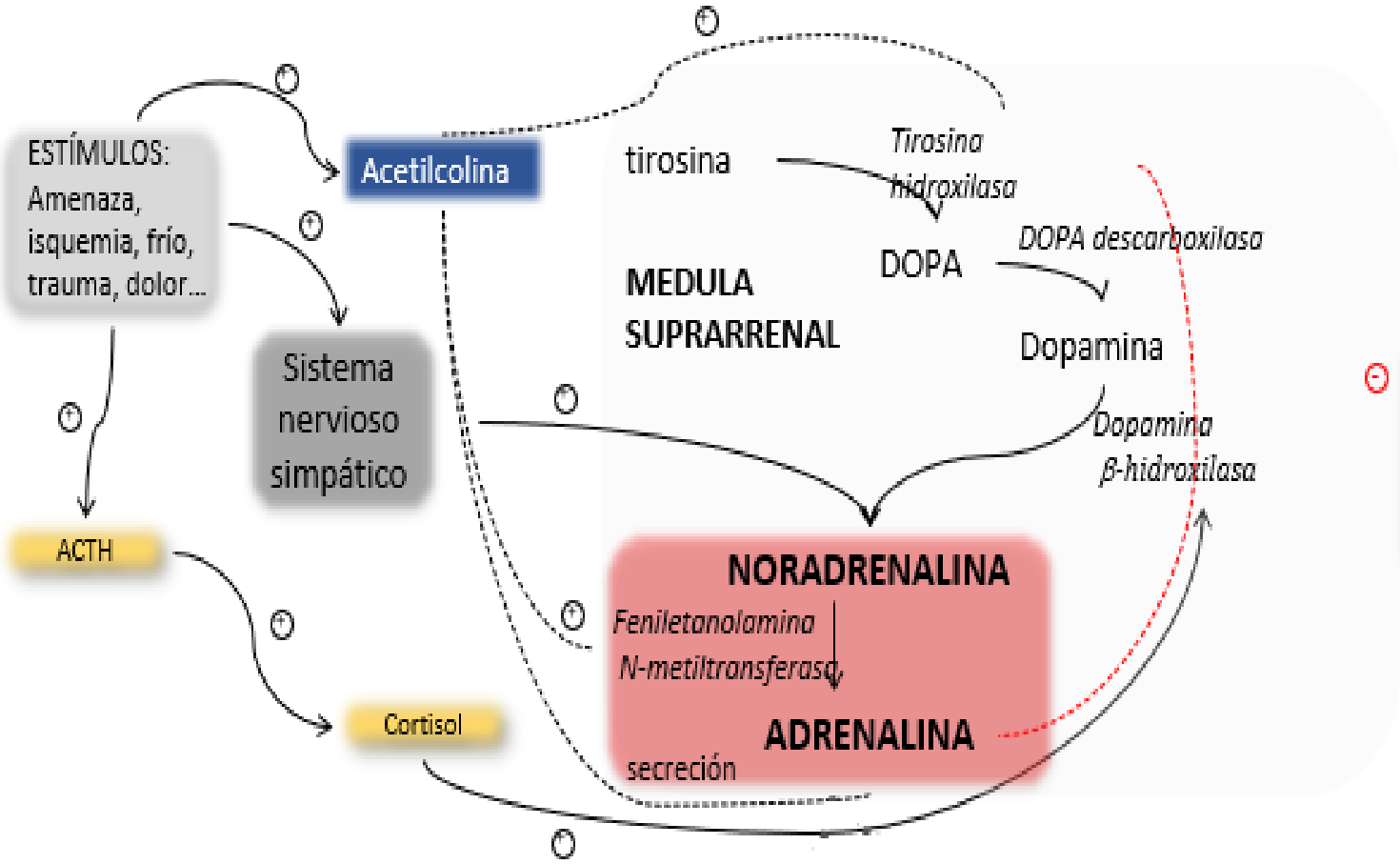
3 School of Physical Education, Sport and Exercise Sciences, University of Otago, Dunedin, New Zealand.

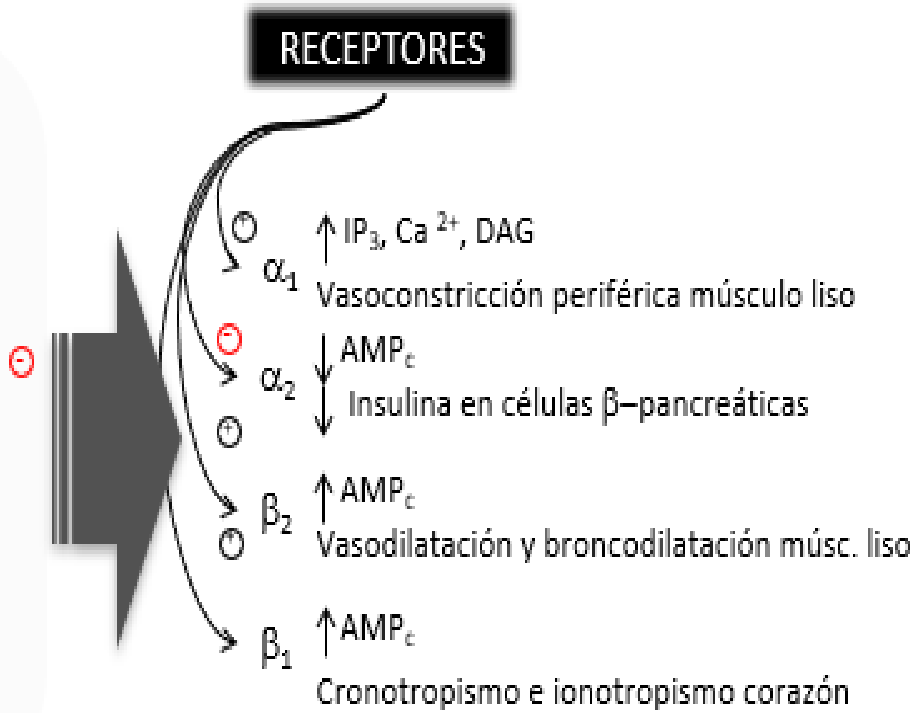
Abstract

The aim of this meta-analysis was to determine the effectiveness of spinal manipulation in influencing various biochemical markers in healthy and or symptomatic population. Electronic databases (n = 10) were searched (from inception till September 2016) and eight trials (325 participants) that met the inclusion criteria were included in the meta-analysis. Two authors independently extracted and assessed the risk of bias in included studies. Standardised mean differences for outcome measures were used to calculate effect sizes. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool was used for assessing the quality of the body of evidence for each outcome of interest. There was moderate quality evidence that spinal manipulation influenced biochemical markers. There was moderate quality evidence of significant difference that spinal manipulation is better (SMD -0.46, 95% CI - 0.93 to 0) than control in eliciting changes in cortisol levels immediately after intervention. There was also a low quality evidence that spinal manipulation is better than control at post-intervention in increasing substance-P (SMD -0.48,95%CI-0.87 to -0.1), neurotensin (SMD -1.8,95%CI-2.56 to -1.04) and oxytocin levels (SMD -2.61,95%CI-3.5to-1.72). However, low quality evidence indicated that spinal manipulation did not influence epinephrine (SMD 0.1,95%CI- 0.56to0.75) or nor-epinephrine levels (SMD -0.06,95%CI-0.71to0.6). The current review found that spinal manipulation can increase substance-p, neurotensin, oxytocin and interleukin levels and may influence cortisol levels post-intervention. However, future trials targeting symptomatic populations are required to understand the clinical importance of such changes.

KEYWORDS: Hormones; Inflammation; Pain markers; Spinal manipulation

CONOCER LA FISIOLOGÍA ES FUNDAMENTAL PARA SABER CUANDO MANIPULAR





Sistemas nervioso endocrino e inmune:

EL EQUIPO PERFECTO

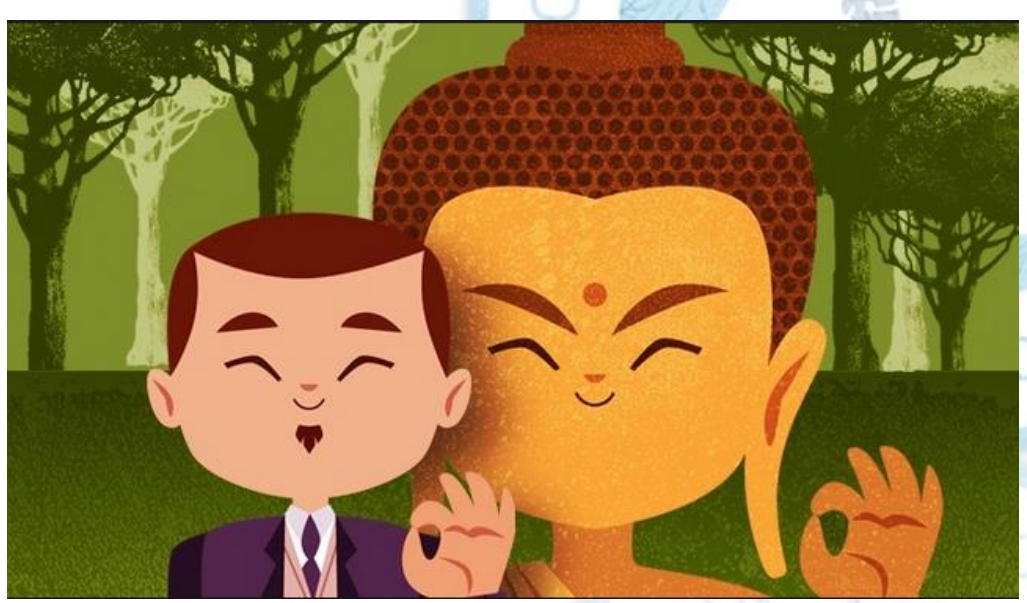
¿QUÉ SABEMOS?: RELACIONES SNV CON SIST ENDOCRINO

- QUE CUALQUIER IRRITACIÓN DEL NOCICEPTOR VISCERAL O SOMÁTICO AFECTA AL SISTEMA INMUNE Y QUE ESTE AFECTA AL VEGETATIVO Y AL ENDOCRINO.

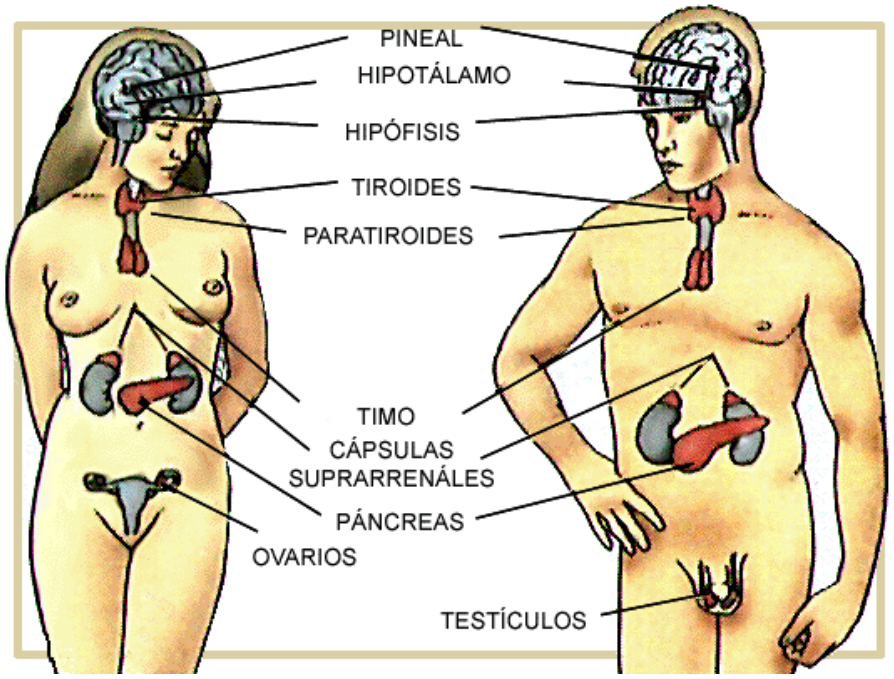
Y ENTONCES… LOS ALUMNOS ME PREGUNTARON → CUANTO DURA EL EFECTO ?

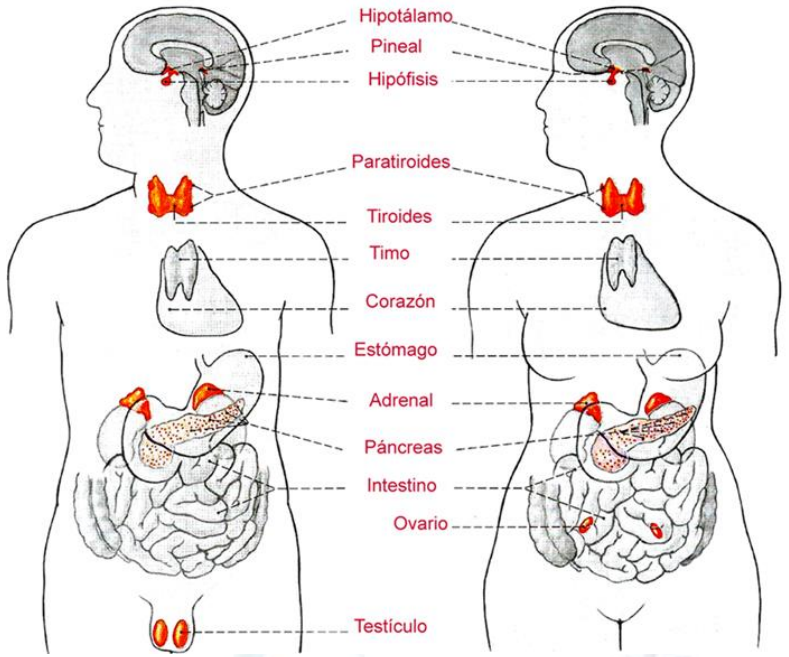
DEGENHART ET AL 2007

Que tras el tratamiento osteopáticos aumentan las Beta endorfinas y se evidencia una activación parasimpática durante 5 días.



ENDOCRINAS- ESTRUCTURA QUÍMICA.





CARÁCTERÍSTICAS	GLÁNDULAS ENDOCRINAS	HORMONAS	FUNCIONES
→ Se originan en las glándulas endocrinas. → Se liberan en la sangre. → Sus efectos se producen en las células blanco, que tienen receptores. → Se clasifican en: **esteroides** (hormonas de la corteza adrenal y las gónadas, derivan del colesterol), **peptídicas** (hormonas del hipotálamo y la hipófisis, hormonas gastrointestinales y hormonas del páncreas; formadas por cadenas de aminoácidos), **monoamínicas** (hormonas de la médula adrenal y tiroideas, se sintetizan a partir de una molécula de aminoácido). → Tienen dos mecanismos de acción: a través de receptores de membrana (hormonas peptídicas y de la médula adrenal, intervención de segundos mensajeros); a través de receptores intracelulares (hormonas esteroides y tiroideas; intervención de proteínas transportadoras, complejos hormona-receptor y efectos sobre el ADN).	Ubicación: cerebro → HIPOTÁLAMO (hormonas liberadoras: TRH, CRH Y GnRH) →HIPÓFISIS → EPÍFISIS	→ Vasopresina, oxitocina (neurohipófisis) → Hormonas trópicas: tirotropina (TSH), corticotropina (ACTH), gonadotropinas (FSH y LH), somatotropina (GH) y prolactina (adenohipófisis). → Melatonina	**Oxitocina**: función reproductora, vínculos entre individuos; **vasopresina**: regulación de líquidos; **H. Trópicas**: actuar sobre otras hormonas para regular su función; **melatonina**: regulación de los ciclos circadianos.
	Ubicación: bajo el cuello → TIROIDES	→ Tiroxina o tetrayodotironina (T4), triyodotironina (T3), calcitonina.	Mantener la tasa metabólica basal, producción de energía, desarrollo normal del SN; **Calcitonina:** metabolismo del Ca.
	Ubicación: bajo los riñones → SUPRARRENALES	→ **Corteza:** mineralocorticoides (aldosterona), glucocorticoides (cortisol). **Médula:** adrenalina, noradrenalina.	**Aldosterona:** regulación de la concentración de iones en sangre; **cortisol y H. de la médula:** reacción ante amenazas y en situaciones de estrés.
	Ubicación: cavidad abdominal → PÁNCREAS	→ Insulina, glucagón.	**Insulina:** transformar exceso de glucosa en glucógeno y grasa; **glucagón:** aumento de glucosa en sangre.
	Ubicación: pelvis → GÓNADAS	→ **Masculinas:** andrógenos (testosterona). **Femeninas:** estrógenos (estradiol) y progesterona.	→ **Andrógenos:** función reproductora masculina e inducción del fenotipo masculino. **Progesterona:** gestación y preparación al embarazo. **Estrógenos:** desarrollo del fenotipo femenino.

6.-INFLAMACIÓN Y SUS RELACIONES CON SNV Y ENDOCRINO.

GRACIAS A MIS ESTUDIOS EN OSTEOPATÍA Y FISIOTERAPIA:

ME CUESTIONÉ LA EFECTIVIDAD DE LOS AINES Y OBTUVE EVIDENCIA CIENTÍFICA DE QUE SU APLICACIÓN A LARGO PLAZO :

1.-DAÑA ORGANOS VITALES.

2.-IMPIDEN LA RECUPERACIÓN Y REGENERACIÓN TISULAR AL INHIBIR LA PGE2.

3.-IMPIDEN LA ACTIVACIÓN DE LAS RESOLVINAS Y LIPOXINAS.

Dakin et al. 2012

Magra and Maffulli, 2006

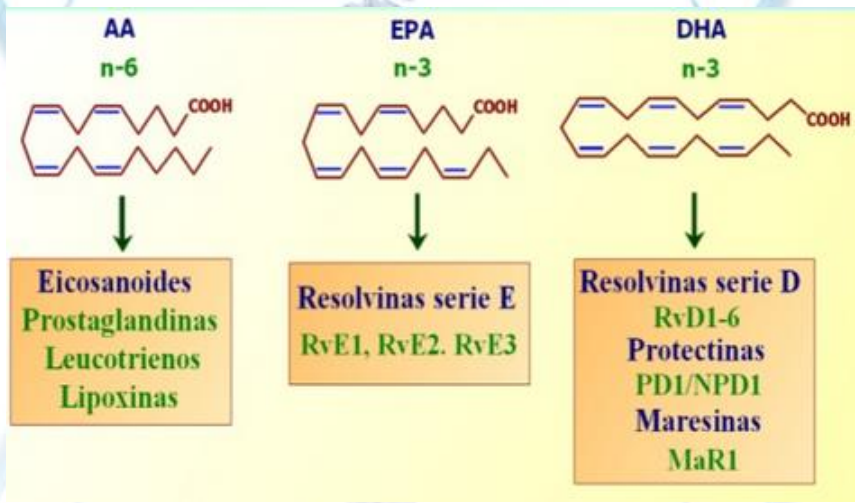
Marsolais et al. 2003.

Clin J Sport Med. 2006 Jan;16(1):1-3.

Nonsteroidal antiinflammatory drugs in tendinopathy: friend or foe.

Magra M, Maffulli N.

PMID: 16377967
[Indexed for MEDLINE]



Rossi, A. G. & Sawatzky, D. A. *The resolution of inflammation (Birkhäuser, Basel , 2008)*

- PGD2 is degraded to 15d-PGJ2 (through COX-2), a strong ligand to PPARγ and has strong anti-inflammatory Properties
- Numerosos estudios han demostrado que los receptores activados por proliferadores de peroxisomas (PPARs) están implicados en varias vías metabólicas tales como la homeostasis glucídica y de lípidos y entre otras en el control de la proliferación y diferenciación celular.
- Los PPARs son factores de transcripción dependientes de ligando que pertenecen a la superfamilia de receptores nucleares hormonales. El nombre de PPAR deriva en los roedores de su capacidad para estimular la proliferación de peroxisomas, organelas que intervienen en la β-oxidación de los ácidos grasos de cadena larga.

Rossi, A. G. & Sawatzky, D. A. *The resolution of inflammation (Birkhäuser, Basel , 2008)*

- PPAR-g se expresa principalmente en el tejido adiposo donde constituye un regulador principal de la diferenciación adipocitaria y participa en la homeostasis glucídica.
- También se expresa en otros territorios como en el riñón y en los vasos sanguíneos por lo que se le ha supuesto un papel en la regulación del tono vascular
- Algunas de las variantes alélicas y mutaciones caracterizadas en el gen PPAR-g humano se han asociado con la obesidad, la hipertensión arterial y la hipertensión arterial relacionada con la obesidad.

PARA DESCUBRIR QUE LA OSTEOPATÍA MODULABA LA INFLAMACIÓN VIA SISTEMA INMUNE , VEGETATIVO Y ENDOCRINO.
PERO….

¿ QUÉ PUEDE GENERAR INFLAMACIÓN?

3.-¿ QUÉ PUEDE GENERAR INFLAMACIÓN?

3.1.- ENVEJECIMIENTO TISULAR :

3.1.1.-ALARGAMIENTO DE LA MOLÉCULA DE ÁCIDO HIALURÓNICO.

El ácido hialurónico tiene un papel importante en la organización de la matriz extracelular. El ácido hialurónico facilitando la absorción de liquido disminuye la viscosidad y facilita el deslizamiento de las fibras de colágeno.

Sin embrago cuando la molécula de ácido hialurónico se alarga mucho se transforma en cadenas muy largas que realizan una zona de adherencias para sustancias proinflamatorias.

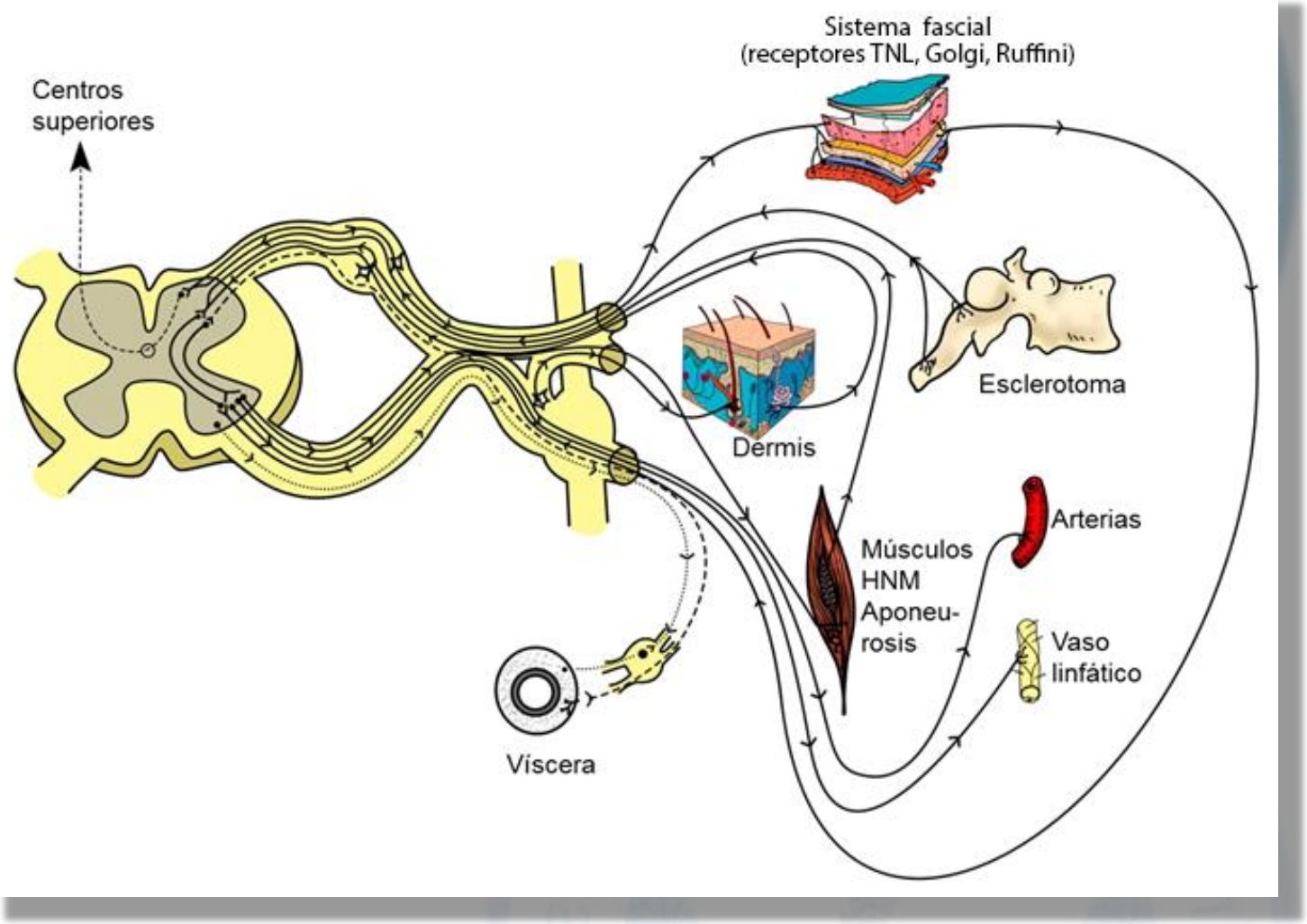
La inflamación altera las fibras de colágeno. Para romper estas cadenas de moléculas de ácido hialurónico anormales utilizamos la presión, la tracción y el calor (Creeping).

Pero en este caso es preciso normalizar el simpático para normalizar la vascularización y eliminar las sustancias proinflamatorias

3.2.- LA FACILITACIÓN MEDULAR , LA SENSIBILIZACIÓN CENTRAL, LA SENSIBILIZACIÓN PERIFÉRICA.

Tenemos que integrar el sistema fascial en el concepto de la facilitación medular de Korr.

EL TRATAMIENTO OSTEOPÁTICO INCLUYE TODOS ESTOS ELEMENTOS!



3.2.-SENSIBILIZACIÓN

Proceso por el que un estímulo normalmente inofensivo es percibido como doloroso (hiperalgesia), por disminución de los umbrales nociceptivos, debido a la amplificación progresiva de la respuesta neuronal tras administraciones repetidas de un estímulo (Erik Kandel, 2000, Premio Nobel).

- **Sensibilización periférica : extensión de la nocicepción en los tejidos inervados por el sistema nervioso periférico.**

- **Sensibilización central :modificación de los umbrales neurales en la médula espinal y/o a la reducción de la inhibición cortical del dolor (plasticidad neuronal).**

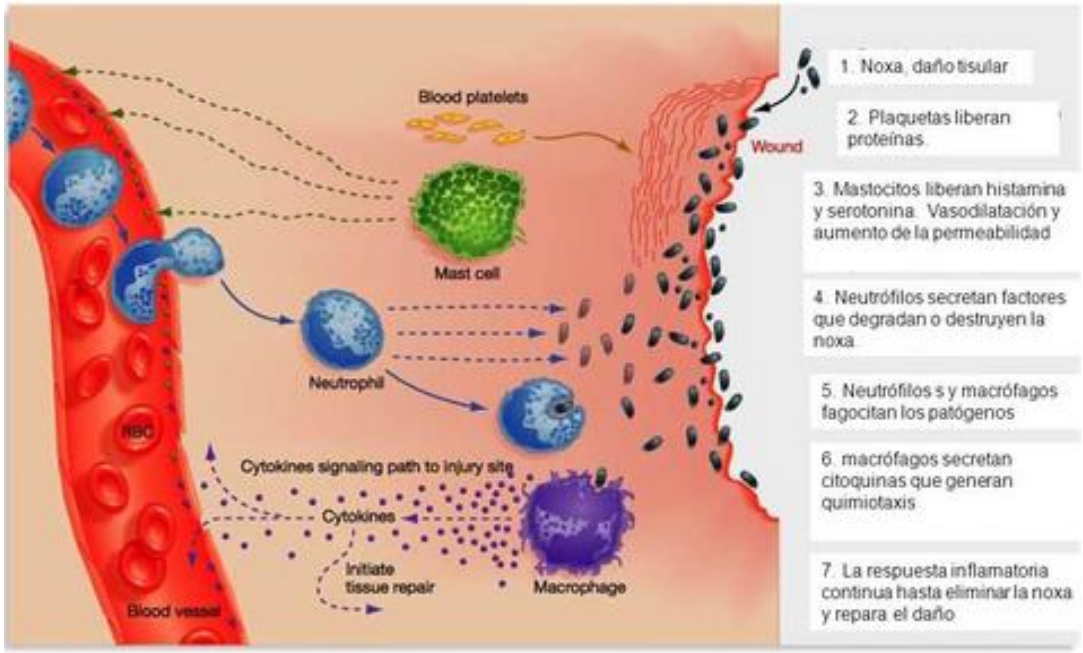
- **Los trenes de impulsos de los nociceptores periféricos tienen la capacidad de desencadenar a largo plazo circuitos en el SNC y pueden causar estados prolongados de hipersensibilidad.**

QUÉ PUEDE GENERAR INFLAMACIÓN: 3.- NOXAS O LESIONES TISULARES. 4.- INFECCIÓN.

Puede producirse por daño y estrés tisular, pero sobre todo por **infección**. Estas serán las señales inflamatorias que indican peligro.

Las vías de la inflamación para producir la enfermedad son las mismas que cuando actúa como mecanismo de defensa anti-infecciosa. El problema es que pueden existir reacciones cruzadas entre el patógeno y elementos propios, lo que dará lugar a trastornos de **autoinmunidad**. Y si durante la adaptación al estrés se produce una alteración de la homeostasis del organismo, se producirán **enfermedades autoinflamatorias**.

Como hemos visto, la **señal de peligro** que pone en marcha la respuesta inflamatoria puede ser endógena o exógena. En condiciones normales, será una **respuesta local** y **controlada**, que tendrá como objetivo la defensa o reparación de los tejidos dañados



Señal inflamatoria
Peligro !!

Infección | Daño tisular | Estrés tisular

Inflamación

Respuesta fisiológica

Defensa anti-infecciosa | Respuesta reparación tejido | Adaptación al estrés, homeostasis

Consecuencias patológicas

Autoinmunidad, inflamación, sepsis | Fibrosis metaplasia, cáncer | Alteración homeostasis Enf autoinflamatoiras

3.4.- INFECCIÓN. Función del macrófago tisular:

1.-Los patógenos que llegan al tejido tras el daño tisular , compiten por los nutrientes de nuestras células y liberan toxinas que dañan aquellas células que no resisten y se fragmentan células.

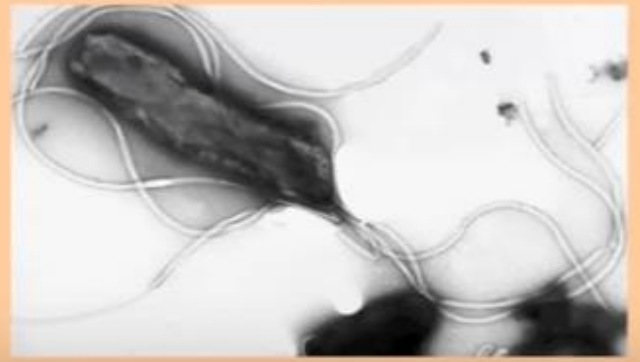
2.-La función del macrófago tisular es la de censar todos los marcadores de daño, chequear el tejido y recopilar información acerca de cómo están las células. **Al recibir estímulos de las células muertas se activa, en el caso de bacterias o restos de las mismas puede fagocitarlas y exponer en su superficie los restos de la bacteria, virus u hongo.**

3.-Al mismo tiempo , las células que han sobrevivido , secretan sustancias (eicosanoides) para avisar al macrófago del daño o la noxa.

- **El macrófago detecta : 1.- restos celulares. 2.- directamente del patógeno. 3.- sustancias secretadas por las células que han sobrevivido.**

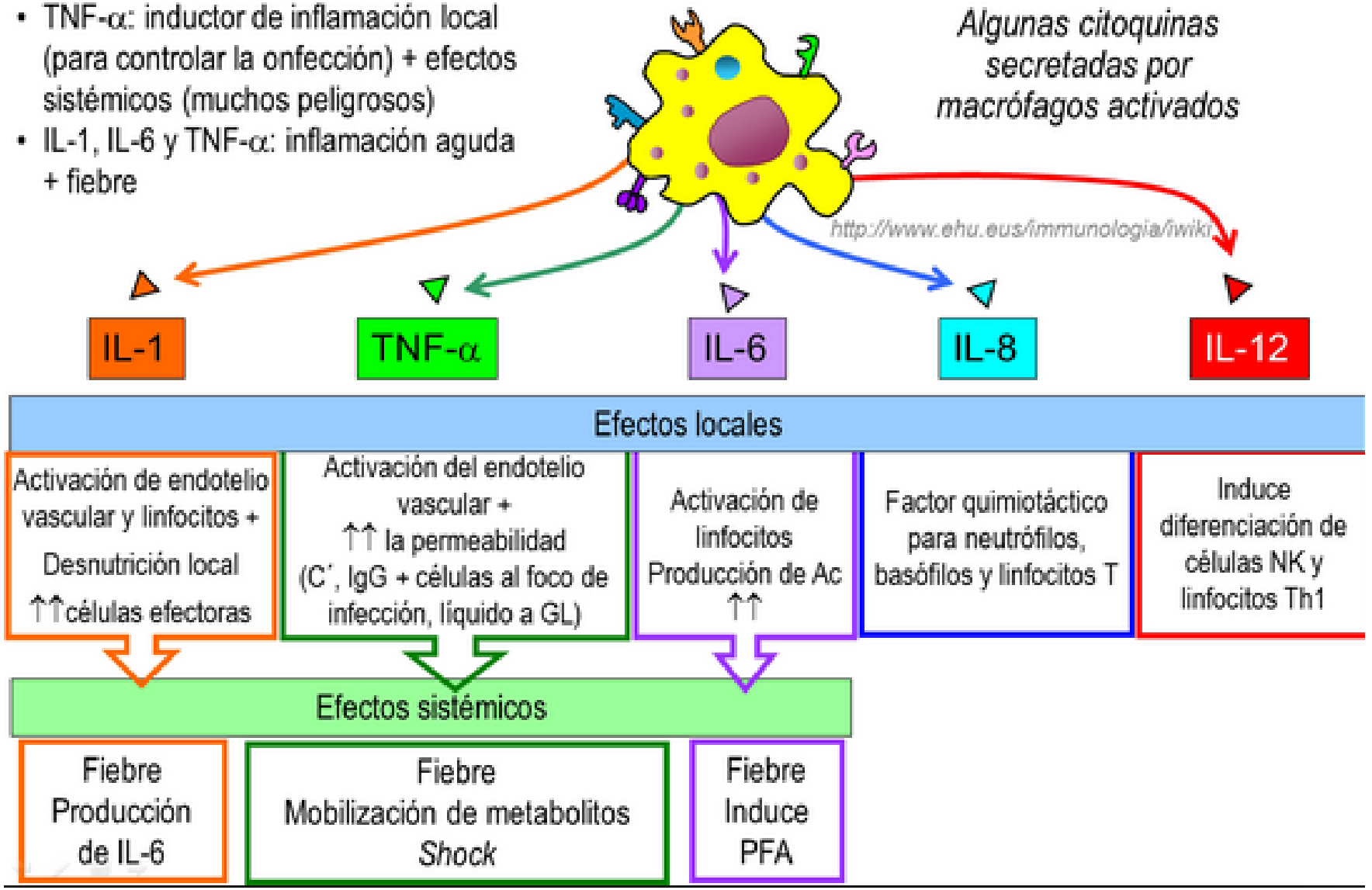
La activación del macrófago , por cualquiera de las tres vías (restos celulares, patógenos ,sust secretadas por células supervivientes)hace que aumente la función de una proteína llamada FACTOR NUCLEAR KAPPA B. NFkB.

PAMP	Receptor
Lipopolisacárido	TLR 4
Lipomananos	TLR 2
Flagelina	TLR 5



DAMP	Receptor
Proteína de choque térmico	TLR 4
ADN en citosol	TLR 9
ADN extracelular	TLR 5
Prostaglandina E_2	EP

- TNF-α: inductor de inflamación local (para controlar la onfección) + efectos sistémicos (muchos peligrosos)
- IL-1, IL-6 y TNF-α: inflamación aguda + fiebre



* FACTOR DE NECROSIS TUMORAL E INTERLEUCINA -1 (TNF ; IL-1)

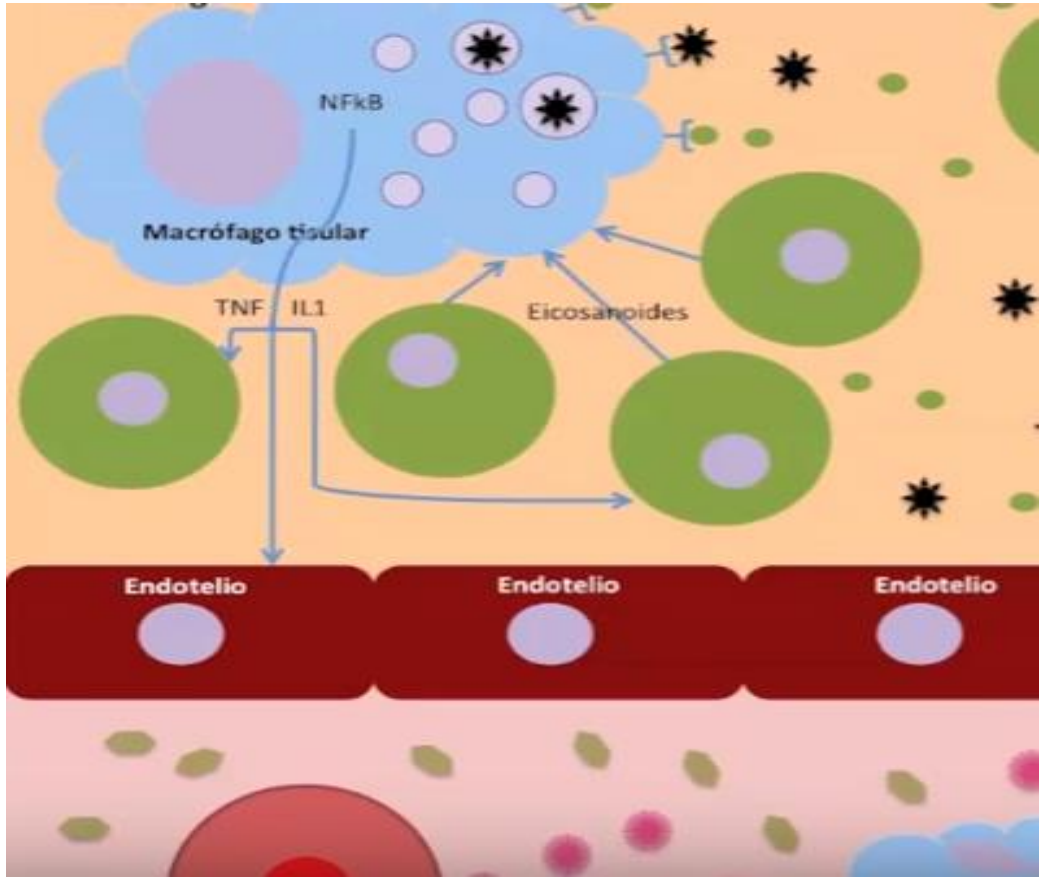
Citocinas principales que median la inflamación.
Se producen en los macrófagos activados.

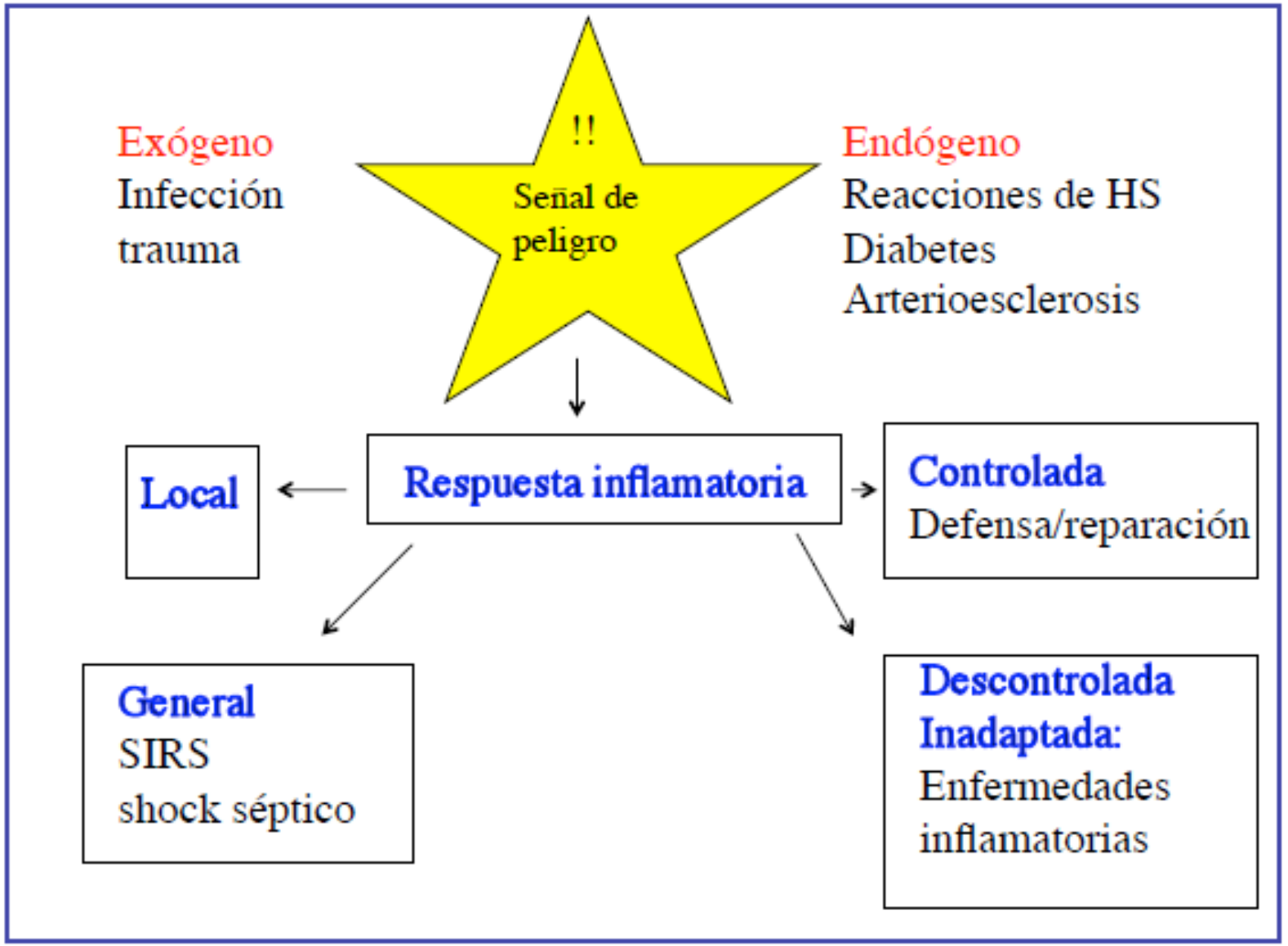
La secreción de TNF e IL-1 se puede estimular por endotoxinas y otros productos microbianos, inmunocomplejos.

TNF aumento de la trombogenicidad del endotelio
provoca agregación plaquetaria

Favorecen la producción de quimioquinas, factores de crecimiento y NO

Principal función : activación endotelial , expresión moléculas adhesión leucocitaria , mayor reclutamiento celular.




Exógeno
Infección
trauma
!!
Señal de peligro
Endógeno
Reacciones de HS
Diabetes
Arterioesclerosis
Local
Respuesta inflamatoria
Controlada
Defensa/reparación
General
SIRS
shock séptico
Descontrolada
Inadaptada:
Enfermedades
inflamatorias

TNF

FasR

ente ATP
s ROS
condria intacta

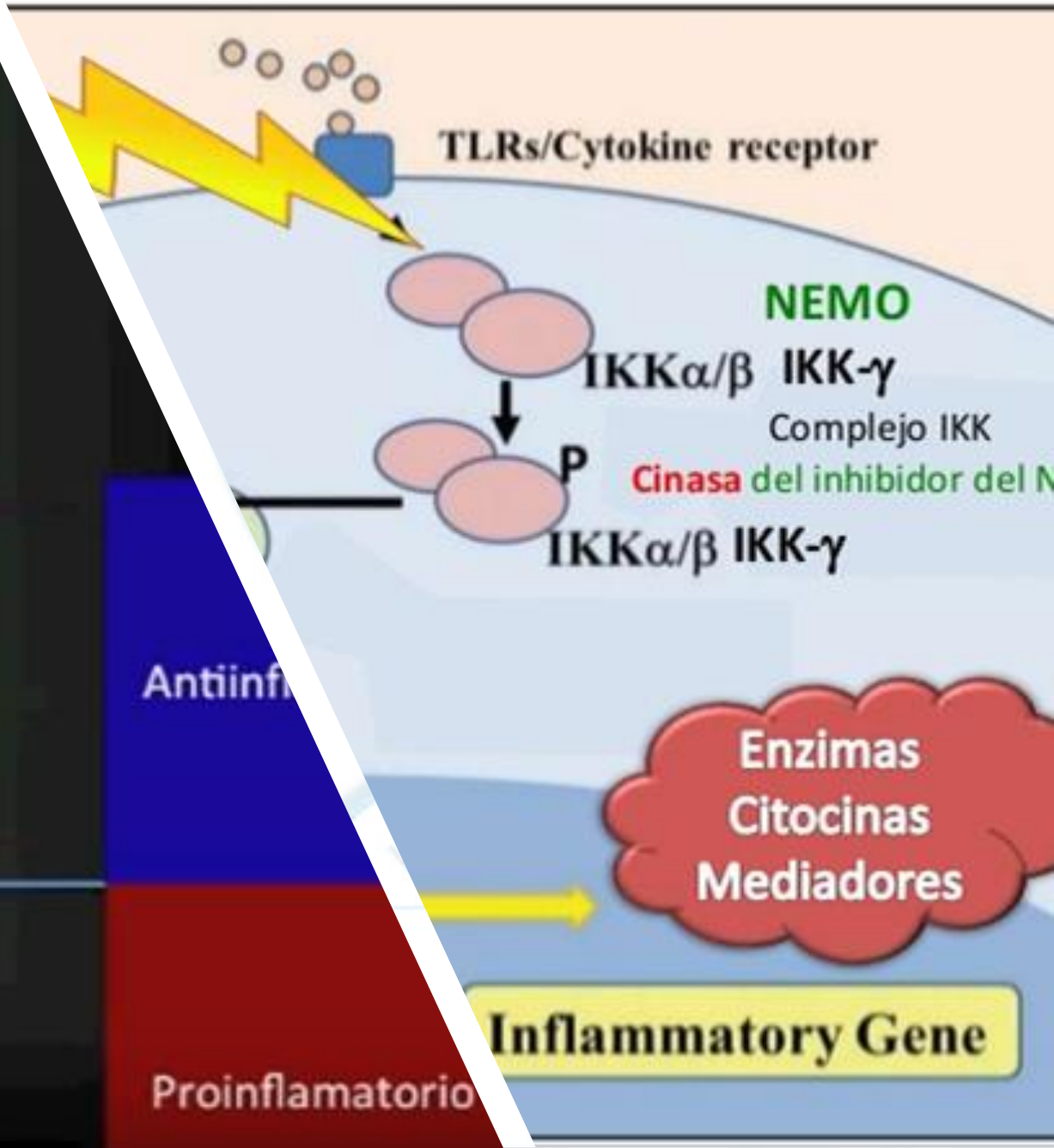
ervivencia celular
HIF, mTOR

Suficiente ATP
Pocas ROS
Mitocondria permeable

Apoptosis
-Caspasa 8, Bax, DIABLO

Depleción de ATP
Muchas ROS
Mitocondria permeable

F-κB → genes pro-inflamatorios



¿ QUÉ ES LA APOPTOSIS?

Apoptosis, muerte celular apoptótica o muerte celular programada

La apoptosis es una vía de destrucción o muerte celular programada o provocada por el mismo organismo, con el fin de controlar su desarrollo y crecimiento, puede ser de naturaleza fisiológica y está desencadenada por señales celulares controladas genéticamente.

La apoptosis tiene una función muy importante en los organismos, pues hace posible la destrucción de las células dañadas, evitando la aparición de enfermedades como el cáncer, consecuencia de una replicación indiscriminada de una célula dañada.

Tejidos dañados o infección

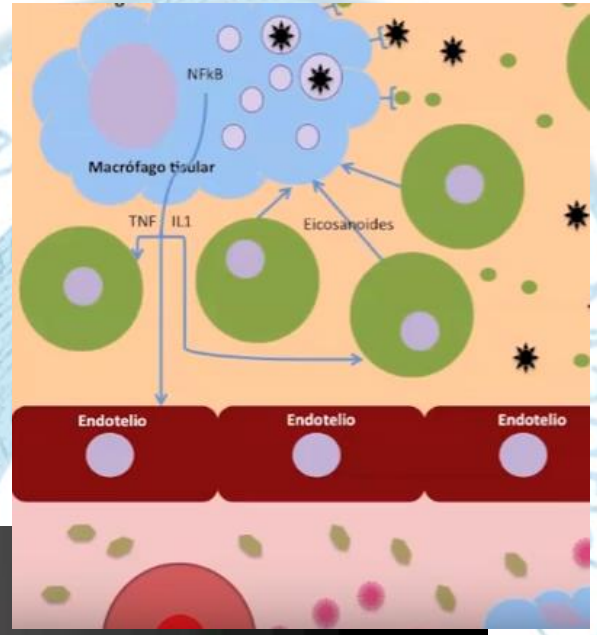
- La apoptosis puede ocurrir, por ejemplo, cuando una célula se halla dañada y no tiene posibilidades de ser reparada, o cuando ha sido infectada por un virus. La "decisión" de iniciar la apoptosis puede provenir de la célula misma, del tejido circundante o de una reacción proveniente del sistema inmunológico. Cuando la capacidad de una célula para realizar la apoptosis se encuentra dañada (por ejemplo, debido a una mutación), o si el inicio de la apoptosis ha sido bloqueado (por un virus), la célula dañada puede continuar dividiéndose sin mayor restricción, resultando en un tumor, que puede ser un tumor canceroso .
- Las células en proceso de apoptosis y sus núcleos se encogen, y con frecuencia se fragmentan. De esta manera, pueden ser eficientemente englobadas vía fagocitosis y, consecuentemente, sus componentes son reutilizados por macrófagos o por células del tejido adyacente.
- Existen dos razones diferentes para explicar por qué las células mueren por apoptosis: La eliminación de células en exceso y la eliminación de células que representan un peligro para la integridad del organismo.

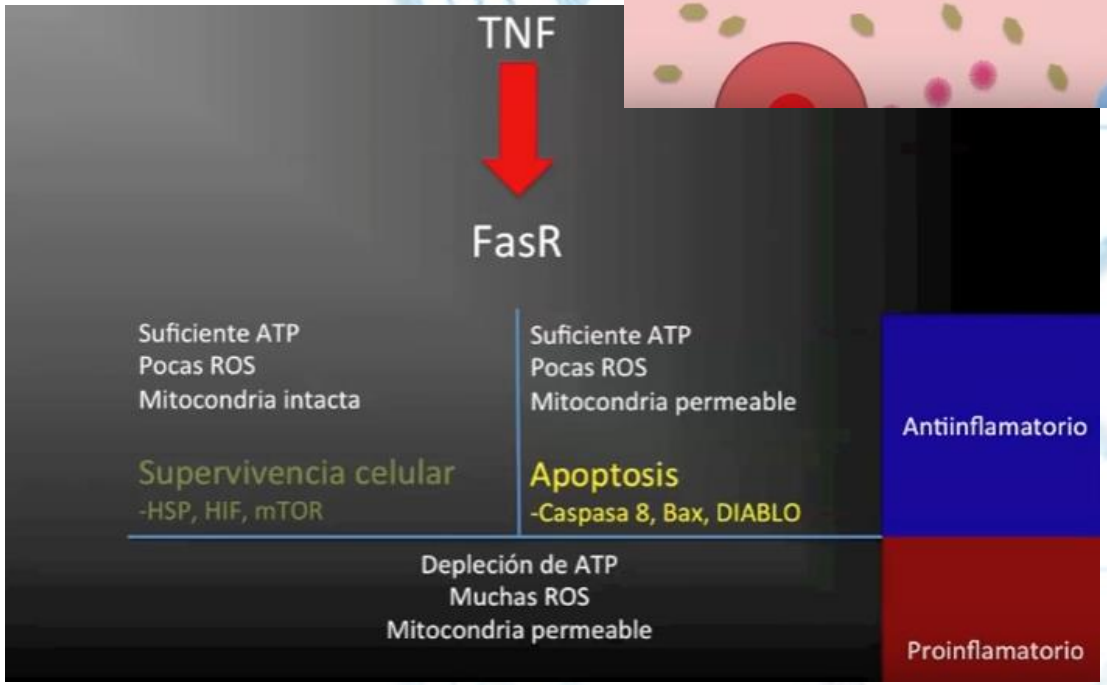
Anti-TNF ALFA. En farmacología se conoce como **anti-TNF** a una sustancia que actúa como inhibidora del Factor de necrosis tumoral (TNF). Algunos tratamientos novedosos en reumatología se basan en el principio de que las citoquinas, como el TNF, necesitan un receptor en la membrana citoplasmática al que ligarse para poder iniciar su acción proinflamatoria, por lo que al bloquear estos receptores específicos del TNF, podría cambiarse el curso de la patología.

- Infliximab
- Adalimumab
- Certolizumab
- Golimumab
- Etanercept

¿QUÉ HACE EL MACRÓFAGO?

- El macrófago tisular censa todos los marcadores de daño tisular-celular, chequear el tejido y recopilar información acerca de cómo están las células.
- En 2017 Liccicardone et al demostraron que tras la manipulación se reduce el TNF ALFA .





Teodorczyk-Injeyan et al. OBSERVARON REDUCCIÓN DEL TNF ALFA TRAS LA MANIPULACIÓN OSTEOPÁTICA.

J Manipulative Physiol Ther. 2006 Jan;29(1):14-21.

Spinal manipulative therapy reduces inflammatory cytokines but not substance P production in normal subjects.

Teodorczyk-Injeyan JA[1], Injeyan HS, Ruegg R.

Author information

1 Division of Research, Canadian Memorial Chiropractic College, Toronto, Ontario, Canada.

Abstract

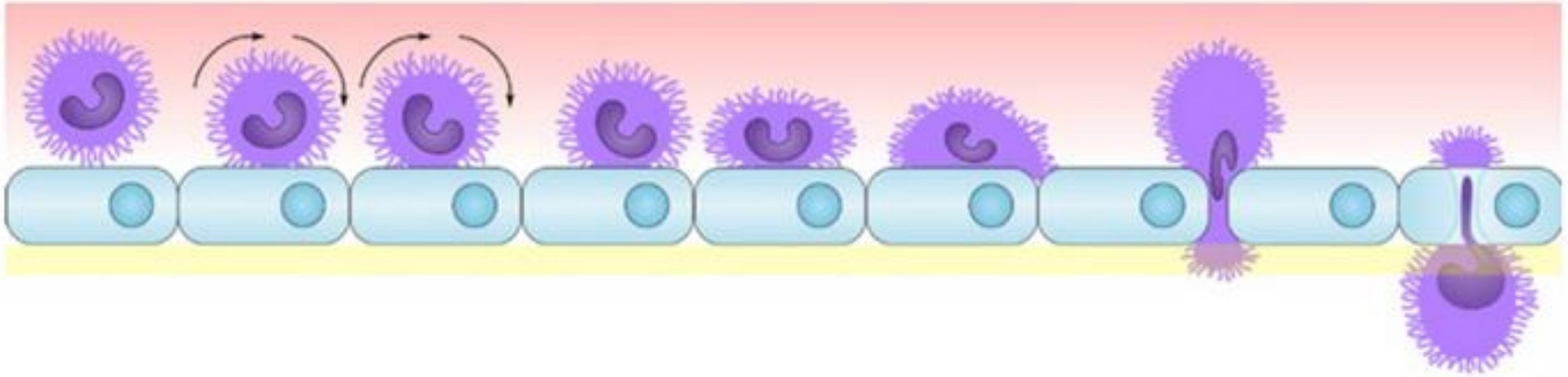
OBJECTIVE: To examine the effect of a single spinal manipulation therapy (SMT) on the in vitro production of inflammatory cytokines, tumor necrosis factor alpha, and interleukin (IL) 1beta, in relation to the systemic (in vivo) levels of neurotransmitter substance P (SP).

METHODS: Sixty-four asymptomatic subjects were assigned to SMT, sham manipulation, or venipuncture control group. SMT subjects received a single adjustment in the thoracic spine. Blood and serum samples were obtained from subjects before and then at 20 minutes and 2 hours after intervention. Whole-blood cultures were activated with lipopolysaccharide (LPS) for 24 hours. Cytokine production in culture supernatants and serum SP levels were assessed by specific immunoassays.

RESULTS: Over the study period, a significant proportion (P </= .05) of sham and control subjects demonstrated progressive increases in the synthesis of tumor necrosis factor alpha and IL-1beta. Conversely, in a comparable proportion of cultures from SMT-derived subjects, the production of both cytokines decreased gradually. Normalization of the observed alterations to reflect the changes relative to self-baselines demonstrated that, within 2 hours after intervention, the production of both cytokines increased significantly (P < .001 to .05) in both controls. In contrast, a significant (P < .001 to .05) reduction of proinflammatory cytokine secretion was observed in cultures from SMT-receiving subjects. In all study groups, serum levels of SP remained unaltered within 2 hours after intervention.

CONCLUSIONS: SMT-treated subjects show a time-dependent attenuation of LPS-induced production of the inflammatory cytokines unrelated to systemic levels of SP. This suggests SMT-related down-regulation of inflammatory-type responses via a central yet unknown mechanism.

Fases	Atraccción al foco inflamatorio	Rodamiento	Adhesión firme	Extravasación leucocitaria o diapédesis	
				Paracelular	Transcelular
Moléculas	Quimiocinas	Selectinas	Integrinas	En migración paracelular: Integrinas de leucocitos y sus ligandos en células endoteliales. Moléculas que se expresan en linfocitos y endotelio (CD31). Complejo VE-cadherina.	



- LAS CÉLULAS DEL ENDOTELIO PRODUCEN INTEGRINAS QUE ATRAPAN PRINCIPALMENTE NEUTRÓFILOS Y LOS INTRODUCEN EN EL TEJIDO DAÑADO. Y LAS QUIMIOCINAS (SECRETADAS POR EL MACRÓFAGO) LE DICEN AL NEUTRÓFILO DÓNDE IR.
- Pero el neutrófilo es superagresivo y ataca a todo. Y genera un ambiente muy ácido y radicales libres y proteasas.
- Se mata mucho pero las células no preparadas mueren y se genera un ambiente inflamatorio.
- El neutrólfilo necesita las citocinas del macrófago para seguir vivo. Cuando destruímos, sólo quedan las supercélulas producidas por el TNF 1. MÁS RESISTENTES AL DAÑO, CONTROLAS LA INVASIÓN , ES LO QUE LLAMAMOS PUS (GENERADO POR LOS NEUTRÓFILOS). AL NO HABER NADA QUE ACTIVE AL MACRÓFAGO SE DEJA DE PRODUCIR TNF E IL, LAS CÉLULAS PASAN A SER NORMALES Y EL ENDOTELIO PASA DE ESTAR ACTIVADO Y NO SE RECLUTAN NEUTRÓFILOS NI PASA LÍQUIDO.

Resolución de la inflamación

Una vez la inflamación ha cumplido su función es necesario que cese. Llega un momento en el que el macrófago cambia y empieza a sintetizar lo contrario: **moléculas antiinflamatorias** (IL4, IL-10, TGFβ…).

La inflamación del tejido se resolverá mediante fibrosis o *ad integrum*.

TGFβ1

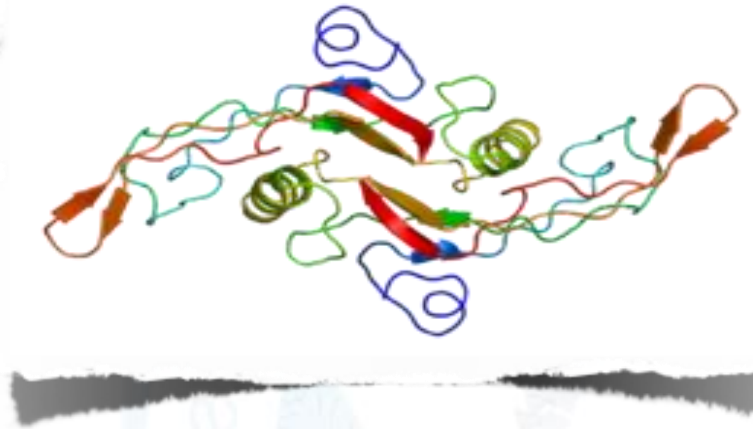
Es un péptido, una molécula compuesta de unos pocos aminoácidos, pertenece a la familia de las citoquinas

Desempeña un papel fundamental en la regulación del sistema inmune, en la regeneración del tejido, la diferenciación celular

La presencia de TGF-1 se deriva de la lesión tisular y la presencia de histamina (es producida por macrófagos /linfocitos y plaquetas + + +)

Estimula los fibroblastos y por lo tanto conduce a la fibrosis

Por lo tanto, un proceso inflamatorio se convierte en un círculo vicioso



Leask A, Abraham DJ. 2004. TGF-beta signaling and the fibrotic response. FASEB J. 18(7):816-27.

Zhongguo Gu Shang. 2019 Apr 25;32(4):377-382. doi: 10.3969/j.issn.1003-0034.2019.04.017.

[Progress on relationship between transforming growth factor-beta1 and tendinopathy].

[Article in Chinese]

Gao F, Li CB, Zhou JB, Shen XZ, Hu B, Lu M, Liu YF, Zhang BQ, Fang YH, Liu YJ[1].

Author information

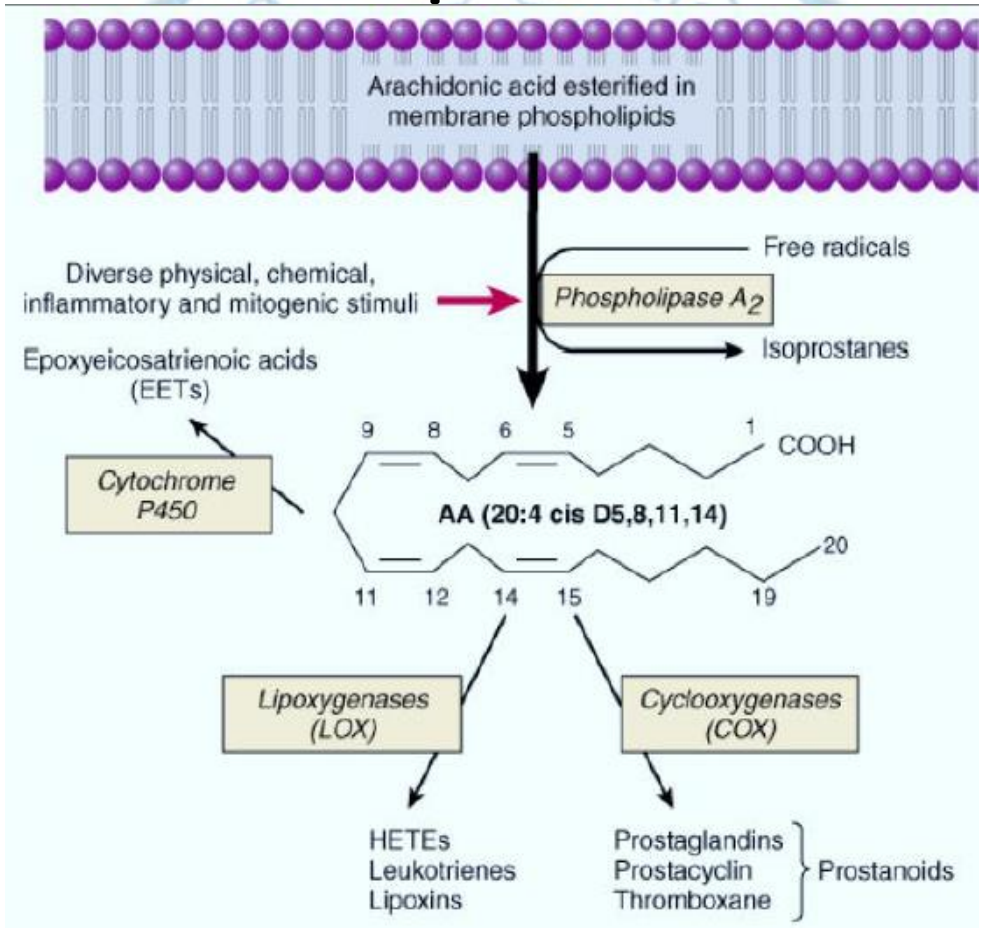
Abstract

As a common soft tissue disease, the mechanism of tendinopathy has not been clarified and is lack of effective treatment method. Change of tissue fibrosis is the one of the main pathological features. Transforming growth factor beta 1 (TGF-β1), which is one of the important factor, participated in fibrosis. Inconsonant expressions of TGF-β1 could be found in tendinopathy. The studies are still controversial, but the vast majority of studies had showed that TGF-β1 was abnormal, and it is given priority to increase, which means that TGF-β1 plays an important role in the process of tendinopathy. In the process of tendon injuries and repairs, the time of TGF-β1 increasing is inconsistent. The time for TGF-β1 plays a significant role has not been determined. TGF-β1 has abnormal expressions in both tendinopathy and tendon repairs, which are two opposite processes. Thus, it may not be a one-way adjustment factor, but has a pleiotropic. Recent studies showed that TGF-β1 was considered as binding to receptor and transferring signal into the cell. Now there are three different receptors are found. The classical pathway of TGF-β1 in intracellular signal transduction is mainly through activation of Smad pathway. In the same time, there are also some non-classical pathways. TGF-β1 could break balance of extracellular matrix, which may be a reason to cause tendinopathy. But the regulations of TGF-β1 on the extracellular matrix are complex and diverse, further studies are required. Existing researches showed that the performance of treatments on tendinopathy is unsatisfied by blocking TGF-β1 downstream pathway. Therefore, it is a good way to study the upstream mechanism of produce TGF-β1. It may be an effective method to find new targets to inhibit the development of tendinopathy better by finding the original source of TGF-β1.

PROBLEMAS DEL TGF BETA (SI NO SE TRABAJA CON READAPTACIÓN O CON TRATAMIENTO DE LA FASCIA)

Prostaglandinas mediadoras en la tendinopatía:

- Las prostaglandinas se sintetizan desde el ácido araquidónico mediante las COX-1 Y COX-2.
- El ácido araquidónico es derivado de la membrana celular fosfolípídica por la actividad de la enzima fosfolipasa en respuesta al trauma, a las citoquinas y a factores de crecimiento(Funk, 2001).
- Las prostaglandinas actúan de modo autocrino y paracrino en concentraciones nanomolares. Las de la serie 2 son las más activas biológicamente. Estos mediadores lipídicos ejercen sus efectos biológicos uniéndose a receptores presentes en la superficie de la membrana celular.
- La producción constitutiva de prostaglandinas es un prerrequisitio para los procesos fisiológicos normales como la remodelación ósea , la vasodilatación y vasoconstricción , la permeabilidad vascular, la agregación plaquetaria o la respuesta de las células tendinosas al movimiento.



(Dunn, 1987; Graham et al., 2009; Petrucci et al., 2011; Saito et al., 1988; Williams, 1979

Science. 2001 Nov 30;294(5548):1871-5.

Prostaglandins and leukotrienes: advances in eicosanoid biology.

Funk CD[1].

Author information

Abstract

Prostaglandins and leukotrienes are potent eicosanoid lipid mediators derived from phospholipase-released arachidonic acid that are involved in numerous homeostatic biological functions and inflammation. They are generated by cyclooxygenase isozymes and 5-lipoxygenase, respectively, and their biosynthesis and actions are blocked by clinically relevant nonsteroidal anti-inflammatory drugs, the newer generation coxibs (selective inhibitors of cyclooxygenase-2), and leukotriene modifiers. The prime mode of prostaglandin and leukotriene action is through specific G protein-coupled receptors, many of which have been cloned recently, thus enabling specific receptor agonist and antagonist development. Important insights into the mechanisms of inflammatory responses, pain, and fever have been gleaned from our current understanding of eicosanoid biology.

PMID: 11729303 DOI: 10.1126/science.294.5548.1871

[Indexed for MEDLINE]

- Como demuestran múltiples estudios la prostaglandina E2($PGE_{2)}$ aumenta en la región peritendinosa aquílea y rotuliana en humanos y ratones sanos, respectivamente, tras el ejercicio in vivo , in vitro o tras lesión(Langberg et al., 1999) (Zhang and Wang, 2010)(Almekinders et al., 1993, 1995; Wang et al., 2004)(Tilley et al., 2001)(Tsuzaki et al., 2003; Yang et al., 2005).

- El papel de las prostaglandinas en la tendinopatía es compleja y diversa con evidencia a favor de efectos deletéreos(PGE_1 →muerte o destrucción celular) y a favor también de efectos beneficiosos.

- EFECTOS DELETEREOS:La inyección peritendinosa de PGE_1 produce cambios degenerativos similares a los observados en las tendinopatías humanas tras 5 semanas de lesión (Sullo et al., 2001).

- EFECTOS BENEFICIOSOS:Parece existir evidencia sobre efectos positivos de la PGE_2 en la curación del tendón. La inyección peritendinosa de 800 ng PGE_2 en tendones rotulianos de ratas mejoró las propiedades mecánicas de los tendones comparado con los controles y con el grupo de inyección de suero salino(Ferry et al., 2012).

- El papel de la PGE, EN ALTAS DOSIS PARECE TENER EFECTOS ANTICATABÓLICOS que antagonizan los efectos catabólicos de la IL-1β (Dakin et al., 2012)

- Los AINES inhiben la producción de prostaglandinas y son agentes farmacológicos ampliamente usados para el tratamiento de las enfermedades inflamatorias y para aliviar el dolor asociado con la tendinopatía.

- A pesar de la evidencia que sugiere que la inflamación tiene efectos perjudiciales para la curación del tejido conectivo, el bloqueo no específico de la respuesta inflamatoria no parece ser beneficioso para el proceso de curación (Magra and Maffulli, 2006; Marsolais et al., 2003).

Clin J Sport Med. 2004 Jul;14(4):232-6.

Prostaglandin E2 affects proliferation and collagen synthesis by human patellar tendon fibroblasts.

Cilli F[1], Khan M, Fu F, Wang JH.

Author information

LA PROSTAGLANDINA E2 AFECTA A LA PROLIFERACIÓN Y PRODUCCIÓN DE COLÁGENO DE LOS FIBROPLASTOS DE MODO DOSIS DEPENDIENTE.

Abstract

OBJECTIVE: To determine the effect of prostaglandin E2 on proliferation and collagen synthesis by human patellar tendon fibroblasts.

DESIGN AND SETTING: Controlled laboratory study.

METHODS: Human patellar tendon fibroblasts were treated with different concentrations (1, 10, 100 ng/mL) of prostaglandin E2 in cultures. Fibroblasts without prostaglandin E2 treatment were used as the control group. The fibroblast proliferation and collagen synthesis were measured using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay and Sircol collagen assay, respectively.

MAIN OUTCOME MEASURED: Changes in proliferation and collagen production of human patellar tendon fibroblasts.

RESULTS: : At 1 ng/mL of prostaglandin E2, there was no significant effect on fibroblast proliferation compared with the control group. At concentrations of 10 ng/mL and 100 ng/mL prostaglandin E2, however, fibroblast proliferation significantly decreased, by 7.3% ($P = 0.002$) and 10.8% ($P < 0.0001$), respectively, compared with the control group. At 1 ng/mL of prostaglandin E2, collagen production of the tendon fibroblasts was unaffected. However, at both 10 ng/mL and 100 ng/mL prostaglandin E2, collagen production was significantly decreased, by 45.2% ($P < 0.0001$) and 45.7% ($P < 0.0001$), respectively, compared with the control group. The levels of collagen production between these 2 dosages did not differ significantly.

CONCLUSIONS: Prostaglandin E2 affects the proliferation of and collagen production by human patellar tendon fibroblasts in a dosage-dependent manner.

CLINICAL RELEVANCE: Based on these in vitro findings, we speculate that production of prostaglandin E2 in tendons might play some role in the acellularity and matrix disorganization seen in exercise-induced tendinopathy.

PMID: 15273529

- La inhibición de la síntesis de prostaglandinas en los fibroblastos del tendón sometidos a estiramiento cíclico *in vitro* genera una elevación compensatoria de los niveles de leukotrieno B_4 un potente marcardor inflamatorio (Li et al., 2004).

- Varios estudios han mostrado el efecto perjudicial en la curación tendinosa y reduciendo la respuesta al ejercicio bloqueando la síntesis de colágeno de los inhibidores de las COX (Cohen et al., 2006; Ferry et al., 2007)(Christensen et al., 2011).

Am J Sports Med. 2004 Mar;32(2):435-40.

Inflammatory response of human tendon fibroblasts to cyclic mechanical stretching.

Li Z[1], Yang G, Khan M, Stone D, Woo SL, Wang JH.

Author information

EL ESTIRAMIENTO CÍCLICO DE LOS FIBROBLASTOS HUMANOS AUMENTA LA PRODUCCIÓN DE PROSTAGLANDINA E2 Y LEUKOTRIENOS B4.

Abstract

BACKGROUND: The cellular and molecular mechanisms for the development of tendinopathy are not clear, but inflammatory mediators produced by tendon fibroblasts in response to repetitive mechanical loading may be an important factor.

HYPOTHESES: (1) Cyclic stretching of tendon fibroblasts affects the production of leukotriene B(4) and the expression of 5-lipoxygenase; and (2) the production level of leukotriene B(4) is inversely related to that of prostaglandin E(2).

STUDY DESIGN: Controlled laboratory study.

METHODS: Human patellar tendon fibroblasts were uniaxially stretched in the presence of indomethacin (25 micro M) or MK-886 (10 micro M). After stretching for 4 hours, followed by 4 hours rest, levels of prostaglandin E(2), leukotriene B(4), and expression of 5-lipoxygenase were measured.

RESULTS: Stretched tendon fibroblasts increased the levels of leukotriene B(4) but did not appreciably change the expression of 5-lipoxygenase. Indomethacin decreased the cellular production of prostaglandin E(2) but caused increased leukotriene B(4) levels. MK-886 caused decreased production of leukotriene B(4) but increased production of prostaglandin E(2).

CONCLUSIONS: Cyclic stretching of human tendon fibroblasts increases the production of prostaglandin E(2) and leukotriene B(4). Blocking prostaglandin E(2) production leads to increased leukotriene B(4) levels and vice versa.

CLINICAL RELEVANCE: The use of nonsteroidal anti-inflammatory drugs for the treatment of tendon inflammation might increase the levels of leukotriene B(4) within the tendon, potentially contributing to the development of tendinopathy.

PMID: 14977670 DOI: 10.1177/0095399703258680

- Además la PGE_2 generada durante la inflamación activa mediadores lipídicos que estimulan la curación como las lipoxinas y resolvinas, que son esenciales en la restauración de la homeostais tisular tras la inflamación o herida (Levy et al., 2001; Serhan et al., 2000a, 2004).

Curr Sports Med Rep. 2011 Sep-Oct;10(5):255-70. doi: 10.1249/JSR.0b013e31822d4016.

Treatment options for patellar tendinopathy: critical review.

Gaida JE[1], Cook J.

Author information

Se afirma que las inyecciones de esteroides son inferiores al ejercicio y no se recomiendan,

Abstract

Patellar tendinopathy is a painful knee injury due to overuse common among jumping athletes. Because rest from sport is neither a feasible nor an effective treatment for patellar tendinopathy in elite athletes, active treatment options are needed. Treatment may be conservative, injection-based, or surgical. This review synthesizes findings from 32 studies of varying quality published between 2001 and 2011. Painful eccentric squats using a 25°-decline board is supported as a first-line treatment. Extracorporeal shock wave therapy is no more effective than placebo. Sclerosing injections seem to be effective, but the evidence is not definitive. Shaving of abnormal tissue via arthroscopic surgery with real-time ultrasound guidance is superior to sclerosing injections. Steroid injections are inferior to exercise interventions and are not recommended. Injections of autologous blood, platelet-rich plasma, and hyperosmolar dextrose are unproven and experimental. Clinicians need to have a comprehensive knowledge of the evidence in the literature, as well as training and experience, when treating patellar tendinopathy.

PMID: 23531972 DOI: 10.1249/JSR.0b013e31822d4016

Clin Sports Med. 2015 Apr;34(2):363-74. doi: 10.1016/j.csm.2014.12.006. Epub 2015 Jan 24.

Treating tendinopathy: perspective on anti-inflammatory intervention and therapeutic exercise.

Joseph MF[1], Denegar CR[2].

Author information

PARECE QUE LOS EJERCICIOS EXCÉNTRICOS SON INTERESANTES PARA LA REPARACIÓN TENDINOSA.

Abstract

Tendinopathy is a common and complex disorder. Once viewed as an inflammatory condition labeled tendinitis, it is now viewed along a continuum that can lead to tissue necrosis and risk of tendon rupture. Anti-inflammatory medications can alter symptoms but may also promote tissue degeneration. Loading of the tendon through exercise, especially exercise involving eccentric muscle contraction, has been shown to promote symptom resolution and functional recovery in many patients. This article reviews the pathoetiology of tendinopathy and the role anti-inflammatory interventions and therapeutic exercise in treatment of active patients.

KEYWORDS: Anti-inflammatory; Eccentric loading; Tendinopathy; Therapeutic exercise

PMID: 25818719 DOI: 10.1016/j.csm.2014.12.006

Unfallchirurg. 2017 Mar;120(3):199-204. doi: 10.1007/s00113-017-0310-9.

[Evidence-based therapy for tendinopathy of the knee joint : Which forms of therapy are scientifically proven?]

[Article in German]

Horstmann H[1], Clausen JD[2], Krettek C[2], Weber-Spickschen TS[3,4].

Author information

Abstract

Tendinopathy in the region of the knee joint is a common pathological disorder. People active in sports, in particular, have a high probability of suffering from tendinopathy. Despite its high clinical relevance, the level of evidence of therapy options for tendinopathy in the knee region differs greatly. This review gives an overview of current evidence levels for therapy options in tendinopathy of the quadriceps, patellar and pes anserinus insertion tendons as well as of the distal iliotibial tract tendon. The treatment with platelet-rich plasma showed a significantly better outcome when used correctly and treatment with shock waves, operative treatment and sclerotherapy have also shown positive effects. Treatment with corticosteroid injections and with oral non-steroidal anti-inflammatory drugs (NSAID) showed positive short-term effects (follow-up ±4 weeks). No reasonable data are available for the treatment of tendinopathy in the knee region by acupuncture, fascial therapy or cryotherapy. The use of kinesio taping showed no significant relief from complaints compared with standard conservative treatment. The use of multimodal therapy without evidence is, therefore, particularly common in elite athletes.

KEYWORDS: Jumpers knee; Level of evidence; Multimodal therapy approaches; Platelet rich plasma; Shock wave therapy

PMID: 28138766 DOI: 10.1007/s00113-017-0310-9

- Por tanto, el bloqueo de las prostaglandinas es probable que tenga un impacto negativo en los mecanismos endógenos del cuerpo para regular la inflamación(Gilroy et al., 1999; Serhan, 2005).

- Las prostaglandinas tienen propiedades inmunomoduladores: por ejemplo PGE_2 regula a la baja la respuesta inflamatoria inhibiendo la producción de IL-12 proinflamatoria y ,a su vez , estimula la producción de la citokina IL-10 antiinflamatoria (van der Pouw Kraan et al., 1995).

La inflamación como vehículo de la curación:

- Una intrigante dimensión de la fisiología de la inflamación es la identificación de mediadores pro resolución como las lipoxinas A_4 (LXA_4) (Serhan et al., 1984) que actúan sobre el receptor de resolvinas FPR2/ALX (Ye et al., 2009) y más recientemente las resolvinas and maresinas (Serhan et al., 2002, 2009). FPR2/ALX se expresa por monocitos y macrófagos (Yang et al., 2001) y es fundamental para controlar la duración y magnitud de la respuesta inflamatoria y provee señales endógenas de stop para la inflamación (Serhan et al., 2000b).

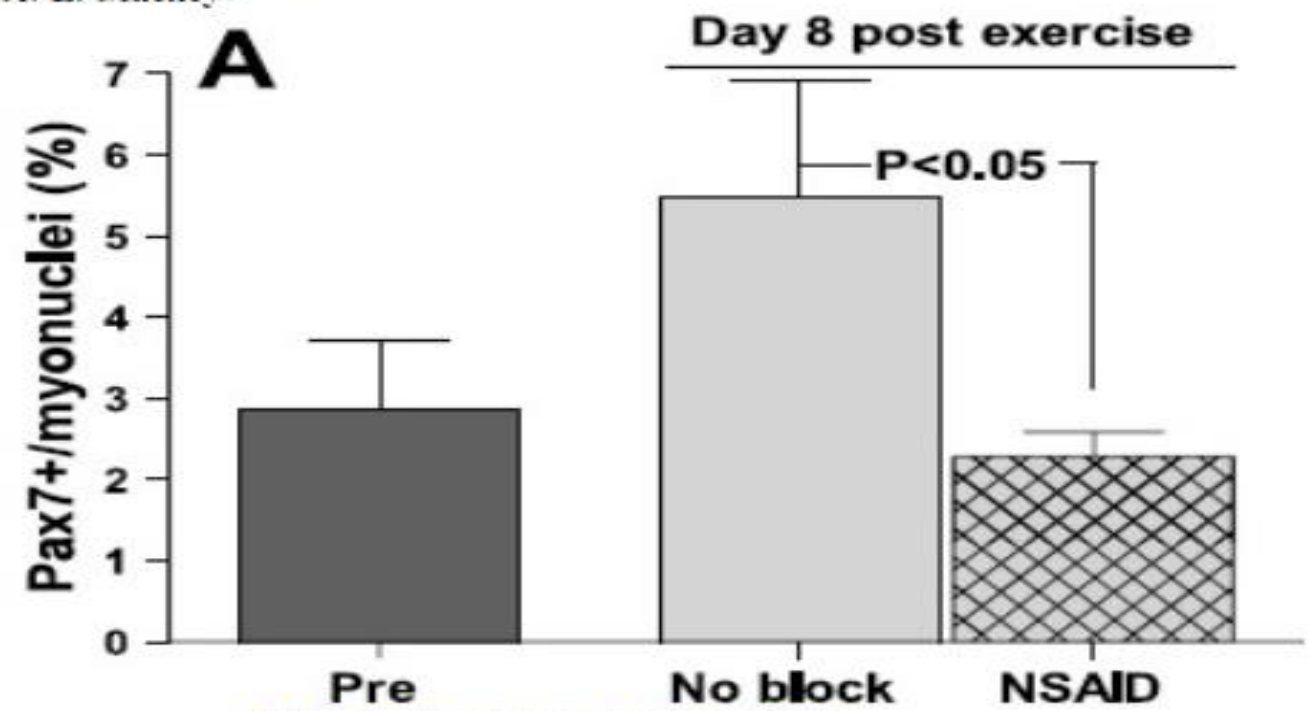
- El uso de esteroides y AINES para aliviar el dolor asociado a la lesión tendinosa es controvertido.

- Mientras que el uso a corto plazo de estas drogas a nivel sistémico no es probable que se asocie con efectos deletéreos , el uso prolongado de aines o la inyección intratendinosa de esteroides se asocia con efectos adversos en las propiedades mecánicas del tendón y propensión a la ruptura (Virchenko et al., 2004) (Shrier et al., 1996).

Local NSAID infusion inhibits satellite cell proliferation in human skeletal muscle after eccentric exercise

U. R. Mikkelsen,[1] H. Langberg,[1] I. C. Helmark,[1] D. Skovgaard,[1] L. L. Andersen,[2] M. Kjær,[1] and A. L. Mackey[1]

Células satélite

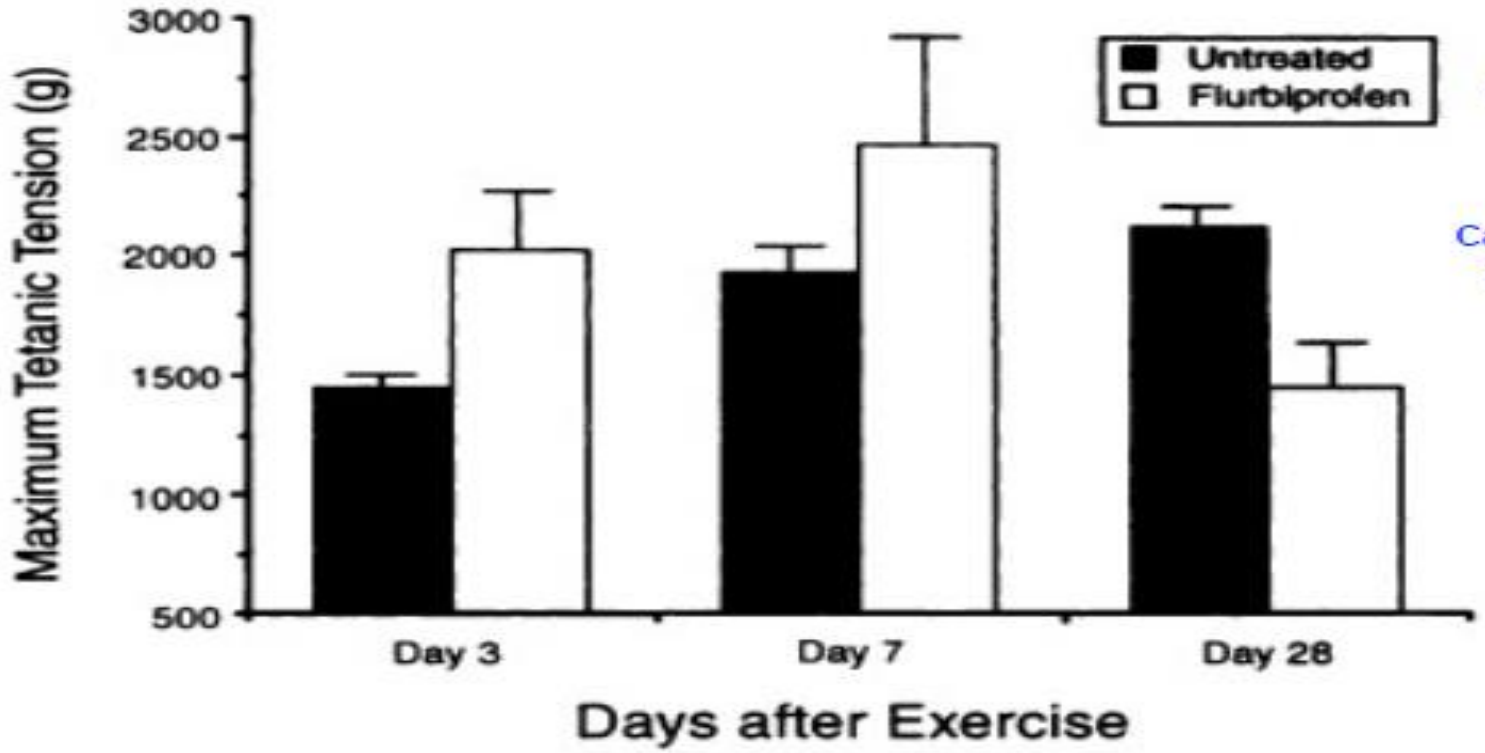


200 contracciones excéntricas
NSAID en una pierna y otra control

J Appl Physiol 107: 1600–1611, 2009

Anti-inflammatory medication after muscle injury. A treatment resulting in short-term improvement but subsequent loss of muscle function

DK Mishra, J Friden, MC Schmitz and RL Lieber
J Bone Joint Surg Am. 1995;77:1510-1519.



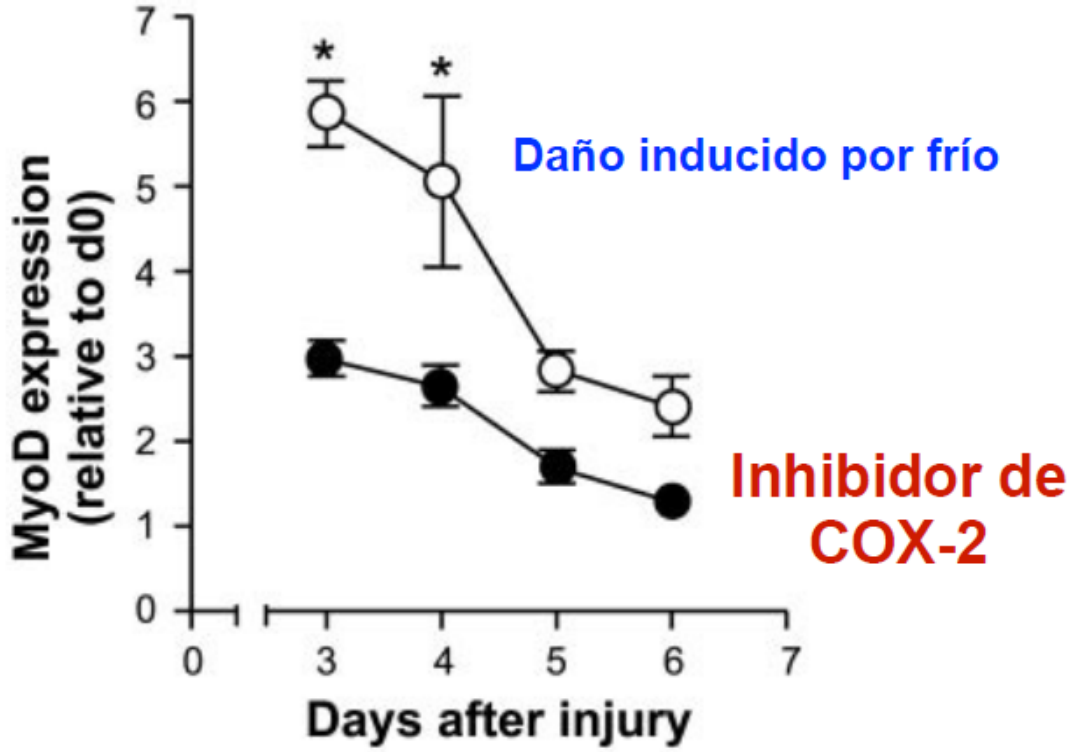
2/día
Durante 6 días

Cada 2seg
30 min

The COX-2 pathway is essential during early stages of skeletal muscle regeneration

Am J Physiol Cell Physiol 287: C475–C483, 2004

Brenda A. Bondesen,[1,2] Stephen T. Mills,[1] Kristy M. Kegley,[1] and Grace K. Pavlath[1]



Cell Physiol Biochem. 2018;50(6):2046-2059. doi: 10.1159/000495050. Epub 2018 Nov 9.

High Concentration of Aspirin Induces Apoptosis in Rat Tendon Stem Cells via Inhibition of the Wnt/β-Catenin Pathway.

Wang Y[1], Tang H[1], He G[1], Shi Y[1], Kang X[1], Lyu J[1], Zhou M[1], Zhu M[1], Zhang J[2], Tang K[3].

Author information

ELEVAR LOS NIVELES DE COX2 TIENE EFECTOS ANTI-APOPTÓTICOS , LA ASPIRINA TIENE EFECTOS PROAPOTÓTICOS

Abstract

BACKGROUND/AIMS: Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used in clinical practice to relieve fever and pain. Aspirin, as a representative NSAID, has been widely used in the treatment of tendinopathy. Some reports have demonstrated that aspirin can induce apoptosis in cancer cells. However, evidence regarding aspirin treatment for tendinopathy, especially the effect of this treatment on tendon stem cells (TSCs), is lacking. Understanding the effect of aspirin on tendinopathy may provide a basis for the rational use of NSAIDs in clinical practice. The aim of our study was to determine whether aspirin induces apoptosis in rat TSCs via the Wnt/β-catenin pathway.

METHODS: First, we used flow cytometry and fluorescence to detect TSC apoptosis. Protein expression of the apoptosis-related caspase-3 pathway was investigated via western blot analysis. Next, we used western blotting to determine the effect of aspirin on the Wnt/β-catenin pathway. We used immunostaining to detect the levels of Bcl2, cleaved caspase-3, and P-β-catenin in the Achilles tendon. Finally, we used flow cytometry, fluorescence, and western blotting to investigate the aspirin-induced apoptosis of TSCs via the Wnt/β-catenin pathway.

RESULTS: Aspirin induced morphological apoptosis in rat TSCs via the mitochondrial/caspase-3 pathway and induced cellular apoptosis in the Achilles tendon. Apoptosis was partly reversed after adding the Wnt signaling activator Wnt3a and lithium chloride (LiCl, a GSK-3β inhibitor). Aspirin administration led to a dose-dependent increase in COX-2 expression. Apoptosis was promoted after adding the COX-2 inhibitor NS398.

CONCLUSION: The Wnt/β-catenin pathway plays a vital role in aspirin-induced apoptosis by regulating mitochondrial/caspase-3 function. Elevating COX-2 levels may protect cells against apoptosis. More importantly, the results remind us to consider the apoptotic effect of aspirin on TSCs and tendon cells when aspirin is administered to treat tendinopathy. The relationship between the positive and negative effects of aspirin remains a subject for future study.

ROLE OF CYCLOOXYGENASE-1 AND -2 IN SATELLITE CELL PROLIFERATION, DIFFERENTIATION, AND FUSION

CHRISTOPHER L. MENDIAS, MS,[1,2] RYUICHI TATSUMI, PhD,[3] and RONALD E. ALLEN, PhD[2]

- Células en cultivo 96 h
- Inhibición selectiva de COX-2 disminuye proliferación de células satélite
- Inhibición de COX-1 y COX-2 reduce diferenciación y fusión de células satélite

Muscle Nerve 30: 497–500, 2004

Cell Prolif. 2009 Dec;42(6):721-30. doi: 10.1111/j.1365-2184.2009.00639.x. Epub 2009 Aug 25.

Aspirin induces apoptosis in mesenchymal stem cells requiring Wnt/beta-catenin pathway.

Deng L[1], Hu S, Baydoun AR, Chen J, Chen X, Cong X.

Author information

Abstract

BACKGROUND AND OBJECTIVES: Mesenchymal stem cells (MSC) are multipotent progenitor cells that are have found use in regenerative medicine. We have previously observed that aspirin, a widely used anti-inflammatory drug, inhibits MSC proliferation. Here we have aimed to elucidate whether aspirin induces MSC apoptosis and whether this is modulated through the Wnt/beta-catenin pathway.

MATERIALS AND METHODS: Apoptosis of MSCs was assessed using Hoechst 33342 dye and an Annexin V-FITC/PI Apoptosis Kit. Expression of protein and protein phosphorylation were investigated using Western blot analysis. Caspase-3 activity was detected by applying a caspase-3/CPP32 Colorimetric Assay Kit.

RESULTS: In these MSCs, aspirin induced morphological changes characteristic of apoptosis, cytochrome c release from mitochondria, and caspase-3 activation. Stimulating the Wnt/beta-catenin pathway by both Wnt 3a and GSK-3beta inhibitors (LiCl and SB 216763), blocked aspirin-induced apoptosis and protected mitochondrial function, as demonstrated by decreased cytochrome c release and caspase-3 activity. Aspirin initially caused a time-dependent decrease in COX-2 expression but subsequently, and unexpectedly, elevated the latter. Stimulation of COX-2 expression by aspirin was further enhanced following stimulation of the Wnt/beta-catenin pathway. Application of the COX-2 inhibitor NS-398 suppressed elevated COX-2 expression and promoted aspirin-induced apoptosis.

CONCLUSION: These results demonstrate that the Wnt/beta-catenin pathway is a key modulator of aspirin-induced apoptosis in MSCs by regulation of mitochrondrial/caspase-3 function. More importantly, our findings suggest that aspirin may influence MSC survival under certain conditions; therefore, it should be used with caution when considering regenerative MSC transplantation in patients with concomitant chronic inflammatory diseases such as arthritis.

PMID: 19706045 DOI: 10.1111/j.1365-2184.2009.00639.x

¿Qué ofrece la Osteopatía para la reparación tendinosa?

Microsc Res Tech. 2007 Apr;70(4):310-24.

Studies on the importance of sympathetic innervation, adrenergic receptors, and a possible local catecholamine production in the development of patellar tendinopathy (tendinosis) in man.

Danielson P[1], Alfredson H, Forsgren S.

⊕ **Author information**

Abstract

Changes in the patterns of production and in the effects of signal substances may be involved in the development of tendinosis, a chronic condition of pain in human tendons. There is no previous information concerning the patterns of sympathetic innervation in the human patellar tendon. In this study, biopsies of normal and tendinosis patellar tendons were investigated with immunohistochemical methods, including the use of antibodies against tyrosine hydroxylase (TH) and neuropeptide Y, and against alpha1-, alpha2A-, and beta1-adrenoreceptors. It was noticed that most of the sympathetic innervation was detected in the walls of the blood vessels entering the tendon through the paratendinous tissue, and that the tendon tissue proper of the normal and tendinosis tendons was very scarcely innervated. Immunoreactions for adrenergic receptors were noticed in nerve fascicles containing both sensory and sympathetic nerve fibers. High levels of these receptors were also detected in the blood vessel walls; alpha1-adrenoreceptor immunoreactions being clearly more pronounced in the tendinosis tendons than in the tendons of controls. Interestingly, immunoreactions for adrenergic receptors and TH were noted for the tendon cells (tenocytes), especially in tendinosis tendons. The findings give a morphological correlate for the occurrence of sympathetically mediated effects in the patellar tendon and autocrine/paracrine catecholamine mechanisms for the tenocytes, particularly, in tendinosis. The observation of adrenergic receptors on tenocytes is interesting, as stimulation of these receptors can lead to cell proliferation, degeneration, and apoptosis, events which are all known to occur in tendinosis. Furthermore, the results imply that a possible source of catecholamine production might be the tenocytes themselves.

PMID: 17206652 DOI: 10.1002/jemt.20413

Histol Histopathol. 2008 Feb;23(2):197-208. doi: 10.14670/HH-23.197.

Immunohistochemical and in situ hybridization observations favor a local catecholamine production in the human Achilles tendon.

Bjur D[1], Danielson P, Alfredson H, Forsgren S.

Author information

Abstract

Results of recent studies using immunohistochemistry show evidence of an occurrence of catecholamine production in the cells (tenocytes) of patellar tendons exhibiting tendinopathy (tendinosis). In the present study, antibodies against the catecholamine-synthesizing enzyme tyrosine hydroxylase (TH) and alpha1-adrenoreceptors were applied to sections of specimens of normal and tendinosis Achilles tendons. In situ hybridization using a probe detecting human TH mRNA was also utilized. It was found that sympathetic innervation was very scarce. On the other hand, there were distinct alpha1-adrenoreceptor immunoreactions in blood vessel walls. Interestingly, tenocytes, particularly from tendinosis samples in which the tenocytes showed an abnormal shape (not the typical slender appearance), displayed TH immunoreactions and reactions for TH mRNA. Of further interest was the finding of alpha1-adrenoreceptor immunoreactions in tenocytes. The observations show not only evidence of local catecholamine production at the protein level, which was the case in recent studies for the patellar tendon, but also at the mRNA level. The observations suggest that the tenocytes, especially those with disfigured appearances in tendinosis, can produce catecholamines and also that they can respond to sympathetic transmitters. This is of interest as adrenergic stimulation in other parts of the body is known to induce degenerative/apoptotic and proliferative events, features which are seen in Achilles tendinosis. These observations are completely new findings concerning the human Achilles tendon. It is likely that locally produced catecholamines and the occurrence of autocrine/paracrine effects of these substances are of great relevance during the process of tendinosis.

PMID: 17999376 DOI: 10.14670/HH-23.197

Front Aging Neurosci. 2016 Aug 9;8:186. doi: 10.3389/fnagi.2016.00186. eCollection 2016.

Role of VEGF, Nitric Oxide, and Sympathetic Neurotransmitters in the Pathogenesis of Tendinopathy: A Review of the Current Evidences.

Vasta S[1], Di Martino A[1], Zampogna B[1], Torre G[1], Papalia R[1], Denaro V[1].

Author information

Abstract

Chronic tendinopathy is a painful common condition affecting athletes as well as the general population undergoing to tendon overuse. Although its huge prevalence, little is known about tendinopathy pathogenesis, and even cloudier is its treatment. Traditionally, tendinopathy has been defined as a lack of tendon ability to overcome stressing stimuli with appropriate adaptive changes. Histologic studies have demonstrated the absence of inflammatory infiltrates, as a consequence conventional antinflammatory drugs have shown little or no effectiveness in treating tendinopathies. New strategies should be therefore identified to address chronic tendon disorders. Angiofibroblastic changes have been highlighted as the main feature of tendinopathy, and vascular endothelial growth factor (VEGF) has been demonstrated as one of the key molecules involved in vascular hyperplasia. More recently, attention has been focused on new peptides such as Substance P, nitric oxide, and calcitonin gene-related peptide (CGRP). Those new findings support the idea of a nerve-mediated disregulation of tendon metabolism. Each of those molecules could be a target for new treatment options. This study aimed to systematically review the current available clinical and basic science in order to summarize the latest evidences on the pathophysiology and its effect on treatment of chronic tendinopathy, and to spread suggestions for future research on its treatment.

KEYWORDS: VEGF; neurotransmitter agents; nitric oxide (NO); nociceptive substance P (SP); tendinopathy; tendons

Comment in

Commentary: Role of VEGF, Nitric Oxide, and Sympathetic Neurotransmitters in the Pathogenesis of Tendinopathy: A Review of the Current Evidences. [Front Aging Neurosci. 2017]

PMID: 27555817 PMCID: PMC4977280 DOI: 10.3389/fnagi.2016.00186

Jewson et al , Alfredson et al y Beccati et al (2019)

Se han observado alteraciones neurovegetativas en la génesis de las alteraciones tendinosas.

El SNV está implicado en la degeneración tisular y tendinosa.

Tendón y ligamento:

Acelerar

LA RECUPERACIÓN

Evidencia Científica

FAVORECER LA REGENERACIÓN TENDINOSA

Effects of Upper and Lower Cervical Spinal Manipulative Therapy on Blood Pressure and Heart Rate Variability in Volunteers and Patients With Neck Pain: A Randomized Controlled, Cross-Over, Preliminary Study.

Win NN[1], Jorgensen AM[1], Chen YS[2], Haneline MT[3].

Author information

Abstract

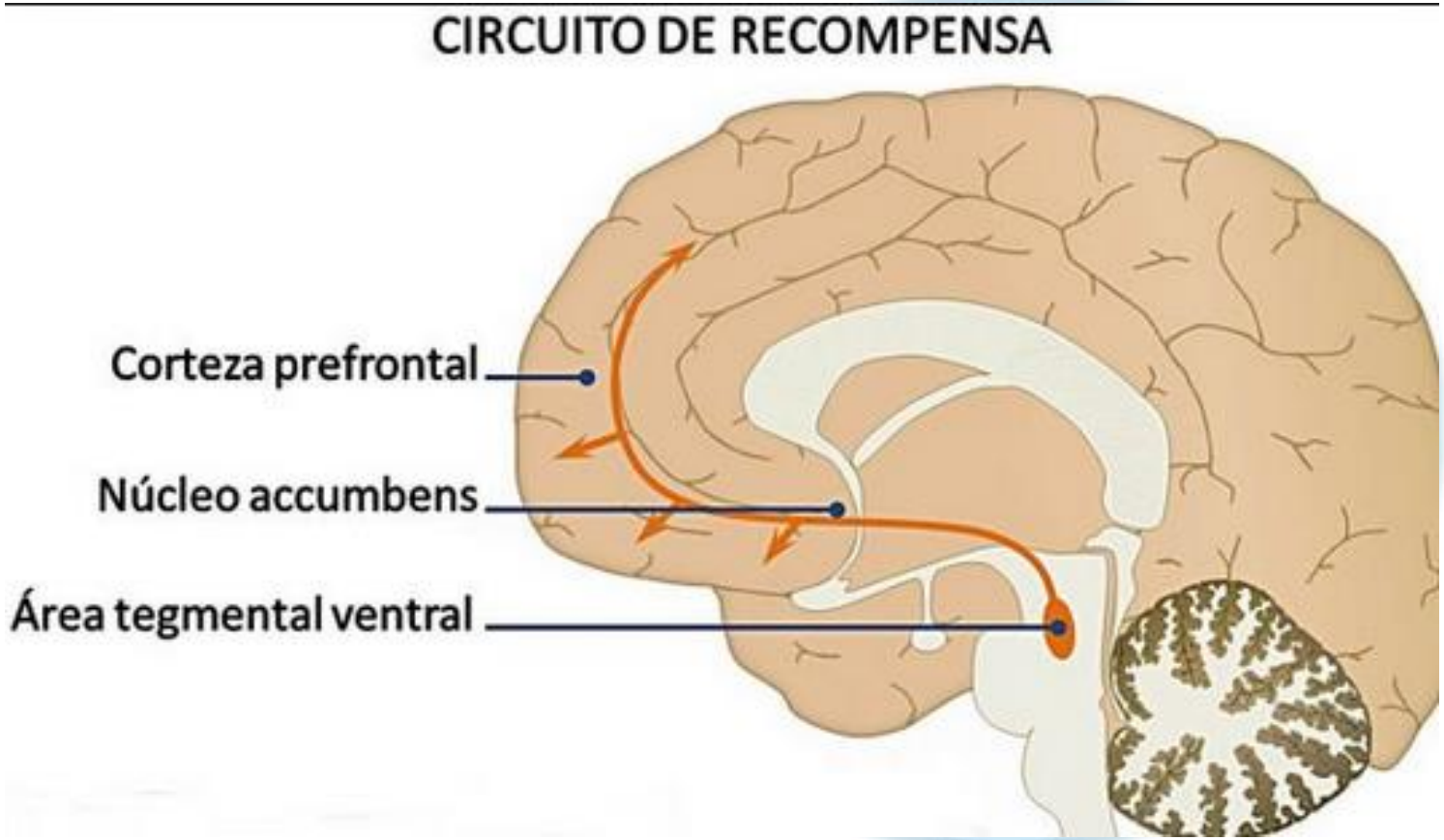
OBJECTIVE: The aims of this study were to examine autonomic nervous system responses by using heart rate variability analysis (HRV), hemodynamic parameters and numeric pain scale (NPS) when either upper (C1 and C2) or lower (C6 and C7) cervical segments were manipulated in volunteers, and whether such response would be altered in acute mechanical neck pain patients after spinal manipulative therapy (SMT).

METHODS: A randomized controlled, cross-over, preliminary study was conducted on 10 asymptomatic normotensive volunteers and 10 normotensive patients complaining of acute neck pain. HRV, blood pressure (BP) and heart rate (HR), and NPS were recorded after upper cervical and lower cervical segments SMT in volunteer and patient groups.

RESULTS: The standard deviation of average normal to normal R-R intervals (SDNN) increased (83.54 ± 22 vs. 105.41 ± 20; P = .02) after upper cervical SMT. The normalized unit of high frequency (nuHF), which shows parasympathetic activity, was predominant (40.18 ± 9 vs. 46.08 ± 14) after upper cervical SMT (P = .03) with a significant decrease (109 ± 10 vs. 98 ± 5) in systolic BP (P = .002). Low frequency to high frequency (LF/HF) ratio, which shows predominance of sympathetic activity increased (1.05 ± 0.7 vs. 1.51 ± 0.5; P = .02) after lower cervical SMT in the healthy volunteers group. However, there was an increase in SDNN (70.48 ± 18 vs. 90.23 ± 20; P = .02 and 75.19 ± 16 vs 97.52 ± 22; P = .01), a decrease in LF/HF ratio (1.33 ± 0.3 vs. 0.81 ± 0.2; P = .001 and 1.22 ± 0.4 vs. 0.86 ± 0.3; P = .02), which was associated with decreased systolic BP (105 ± 10 vs. 95 ± 9; P = .01 and 102 ± 9 vs. 91 ± 10; P = .02) and NPS scores (3 ± 1 vs. 0; P = .01 and 3 ± 1 vs. 1 ± 1; P = .03) following both upper and lower cervical SMT in the patient's group. The baseline HR was 67 ± 9 vs 64 ± 5 (upper cervical) and 65 ± 7 vs 69 ± 11 (lower cervical) in both the healthy volunteer' and patient' groups.

CONCLUSION: Upper cervical SMT enhances dominance of parasympathetic and lower cervical SMT enhances dominance of sympathetic activity in this young volunteer group. However, dominance of parasympathetic activity was found in patients with neck pain that received both upper and lower cervical SMT.

Inami A, Ogura T, Watanuki S, Masud MM, Shibuya K, Miyake M, et al. Glucose Metabolic Changes in the Brain and Muscles of Patients with Nonspecific Neck Pain Treated by Spinal Manipulation Therapy: A [(18)F]FDG PET Study. Evid Based Complement Alternat Med. 2017;2017:4345703.



ACTIVAR ÁREAS CORTICALES RELACCIONADAS CON LA MOTIVACIÓN Y LA RECOMPENSA

Evid Based Complement Alternat Med. 2017;2017:4345703. doi: 10.1155/2017/4345703. Epub 2017 Jan 12.

Glucose Metabolic Changes in the Brain and Muscles of Patients with Nonspecific Neck Pain Treated by Spinal Manipulation Therapy: A [^{18}F]FDG PET Study.

Inami A[1], Ogura T[2], Watanuki S[1], Masud MM[3], Shibuya K[4], Miyake M[1], Matsuda R[1], Hiraoka K[1], Itoh M[4], Fuhr AW[5], Yanai K[6], Tashiro M[1].

Author information

Abstract

Objective. The aim of this study was to investigate changes in brain and muscle glucose metabolism that are not yet known, using positron emission tomography with [^{18}F]fluorodeoxyglucose ([^{18}F]FDG PET). *Methods*. Twenty-one male volunteers were recruited for the present study. [^{18}F]FDG PET scanning was performed twice on each subject: once after the spinal manipulation therapy (SMT) intervention (treatment condition) and once after resting (control condition). We performed the SMT intervention using an adjustment device. Glucose metabolism of the brain and skeletal muscles was measured and compared between the two conditions. In addition, we measured salivary amylase level as an index of autonomic nervous system (ANS) activity, as well as muscle tension and subjective pain intensity in each subject. *Results*. Changes in brain activity after SMT included activation of the dorsal anterior cingulate cortex, cerebellar vermis, and somatosensory association cortex and deactivation of the prefrontal cortex and temporal sites. Glucose uptake in skeletal muscles showed a trend toward decreased metabolism after SMT, although the difference was not significant. Other measurements indicated relaxation of cervical muscle tension, decrease in salivary amylase level (suppression of sympathetic nerve activity), and pain relief after SMT. *Conclusion*. Brain processing after SMT may lead to physiological relaxation via a decrease in sympathetic nerve activity.

PMID: 28167971 PMCID: PMC5267084 DOI: 10.1155/2017/4345703

CONCLUSIÓN:

Hasta ahora no se ha demostrado que ningún medicamento o tratamiento inyectable altere las propiedades del tejido;

Solo la carga CONTROLADA BASADA EN LA EVIDENCIA de LAS ESTRUCTURAS CONECTIVAS ASOCIADA A LA MODULACIÓN DE LA RESPUESTA NEUROVEGETATIVA puede estimular su remodelación.

The challenge of managing tendiopathy in competing athletes. Br J Sports Med. 2014;48:506-9.

¿ QUÉ PUEDE HACER EL OSTEÓPATA ?

LESIÓN	MANIPULACIONES	TRATAMIENTO FASCIA	READAPTACIÓN	Tratamiento dietético y su acción
TENDINOSIS AQUÍLEA	TIBIOTARSIANA. SUBASTRAGALINA. CHOPART Y LISFRANCK. ROTACIÓN TIBIAL. ILIACOS Y SACRO. VERIFICAR CARGAS Y LUMBARES. ATENCIÓN A DESVIACIONES POR OJO, BOCA O PIE. TRABAJO 4º VENTRÍCULO, TRABAJO ARP, VAGO, TRABAJO VISCERAL, TRABAJO SNV, TRABAJO SISTEMA LEMNISCAL Y EXTRALEMNISCA.	VENDA GASTROPLANTAR. FASCIAL PLANTAR. AQUILES Y SEPTOS . GEMELOS , SÓLEO Y TIGOCO. IMPORTANCIA VERIFICAR CADENAS Y CRÁNEO-SACRO.	TRABAJO ISOMÉTRICO 3 SEMANAS (ACORTAMIENTO O ESTIRAMIENTO DEPENDIENDO DE MODALIDAD DEPORTIVA). PASAMOS A CONCÉNTRICOS O EXCÉNTRICOS (VER JILL COOK Y E.RIO), EJERCICIOS FUNCIONALES MULTIAXIALES Y CONTROL MOTOR.	PISTACHOS. LISISNA/ GLICINA(EN PISTACHO) VIT C. HIERRO. MAGNESIO. ZINC. CONTROL GLUCEMIA Y COLESTEROL. MELATONINA.
APLICAR MISMA LÓGICA A CUADRICIPITAL Y RESTO				

ADEMÁS….

- LA OSTEOPATÍA PUEDE REFORZAR LAS MEDICACIONES ANTIRREUMÁTICAS:

CORTICOESTEROIDES.

ANTI TNF.

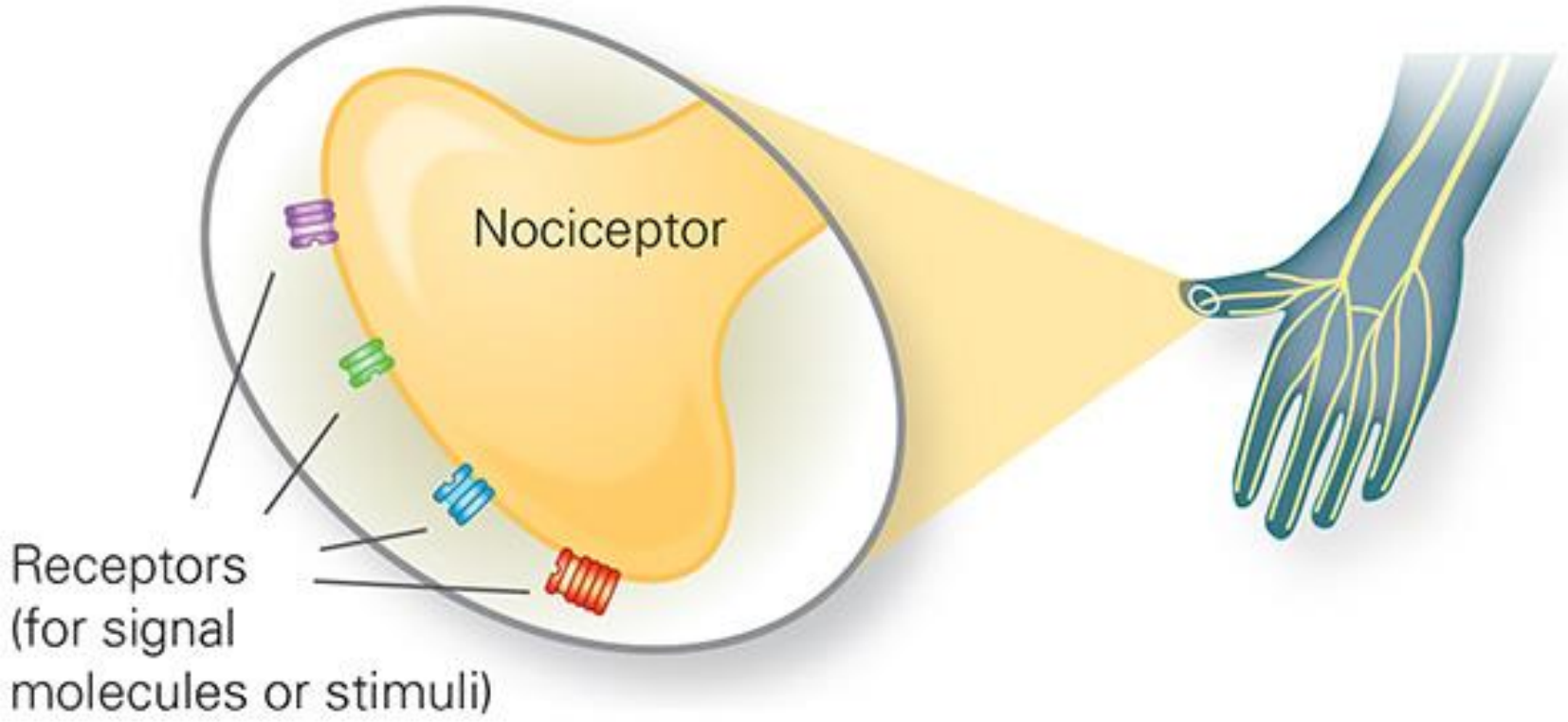
LA OSTEOPATÍA PUEDE REFORZAR LAS MEDICACIONES ANTI GOTOSAS (COLCHICINA, ALOPURINOL).

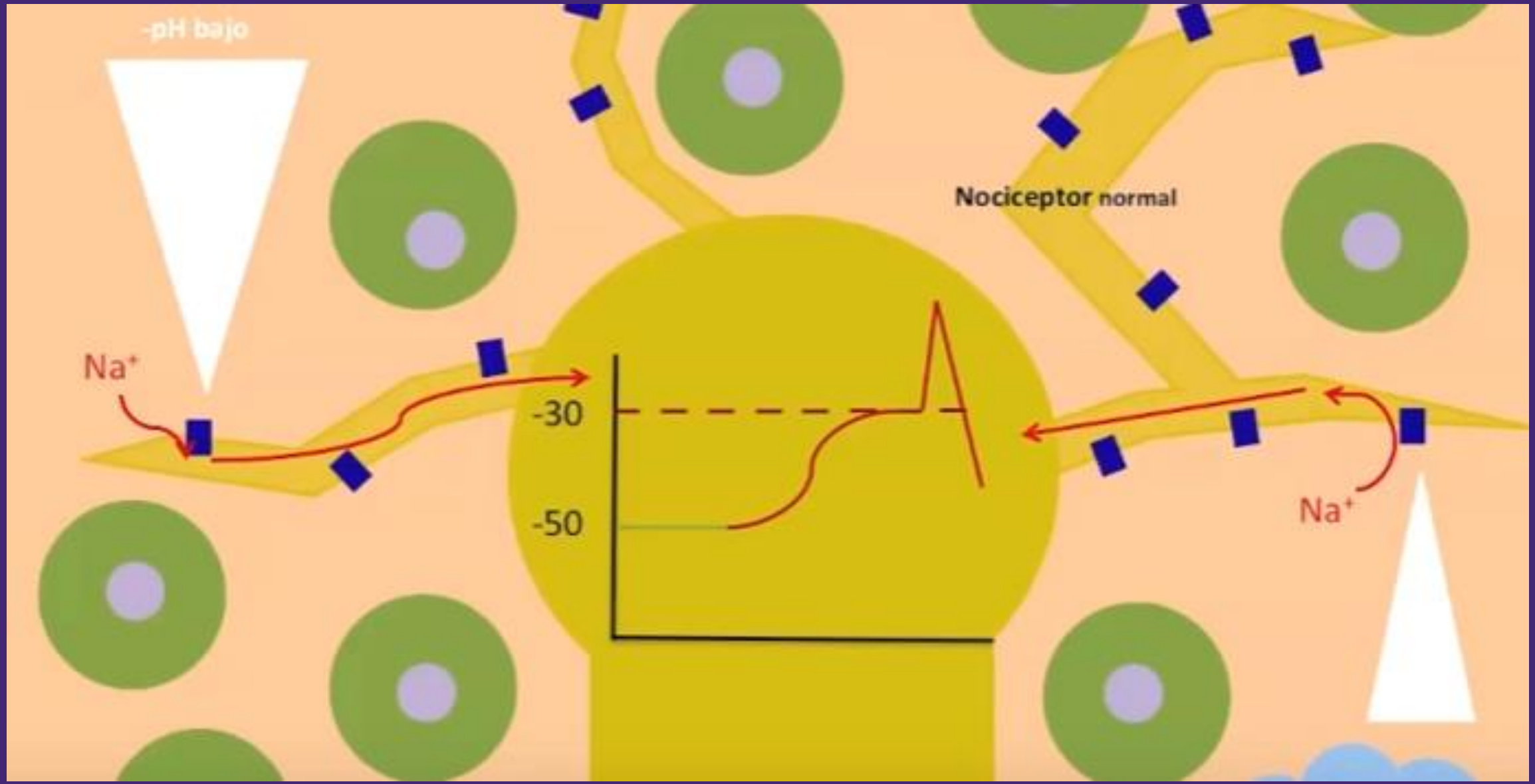
LA OSTEOPATÍA PUEDE REFORZAR EL EFECTO DE OPIOIDES, LAXANTES, BENZODIACEPINAS, CONCERTA, RITALÍN,AINES…

QUÉ PUEDE GENERAR INFLAMACIÓN: 5.-irritación del nociceptor. El dolor

Aquí nos encontramos con una interesante situación. La respuesta del macrófago tisular es la misma ante una noxa lesiva que genera sustancias o restos celulares , con la consiguiente inflamación y dolor, y responde análogamente si el nociceptor irritado recluta al macrófago .

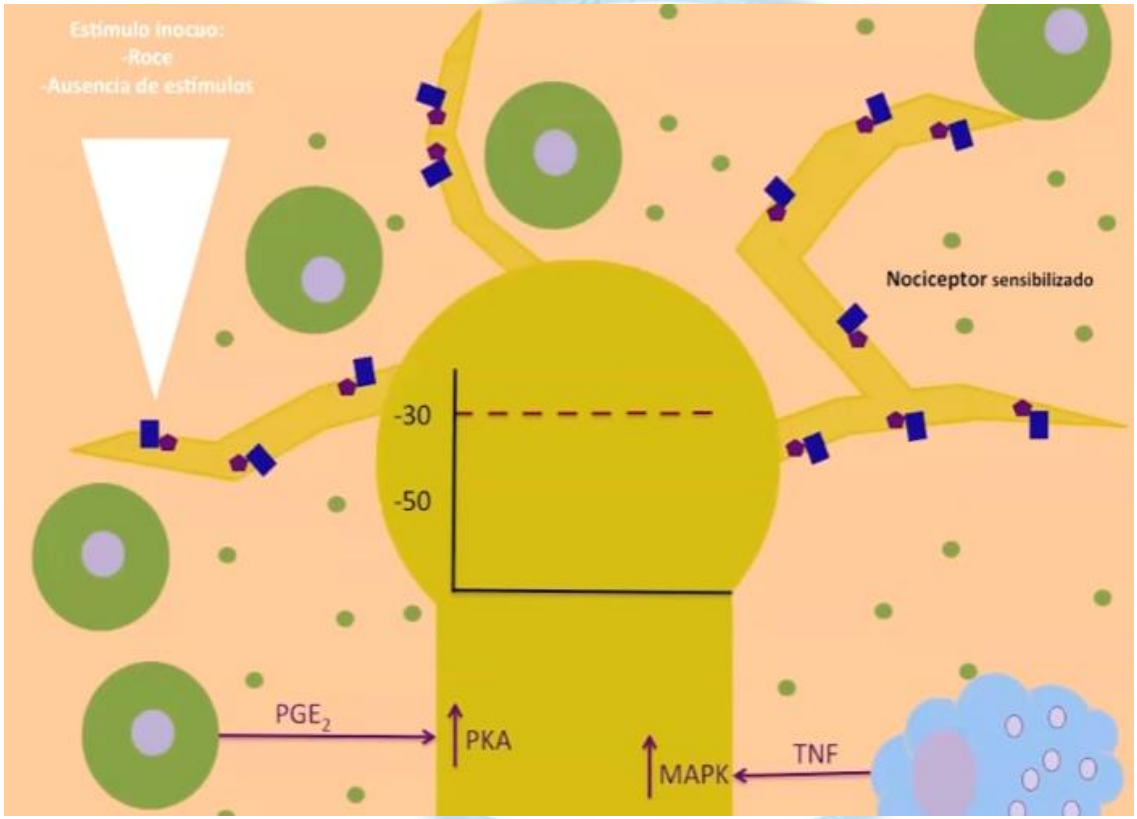
Nociceptors, our "pain sensors"




-pH bajo
Nociceptor normal
Na+
-30
-50
Na+

Ahora el receptor ya no funciona como antes , sino que está sensibilizado y . Ante un estímulo leve , como el roce , va a generar una despolarización neural.

A este proceso en que el receptor está sensibilizado lo llamamos hiperalgesia o alodinia (cuando , incluso el roce o la ausencia de estímulos genera el dolor).
Los receptores mínimamente estimulados se abren , y también los no estimulados. Esto genera muchas corrientes de despolarización , entra mucho más sodio y mucho más tiempo. Paso de tener un potencial de acción por estímulo a tener una gran cantidad de potenciales de acción. Tocas una vez y te duele 100 veces (como si hubieras tocado 100 veces).



Receptor	Modalidad Sensorial	Estímulo específico	Mediador	Principal Efecto
EP2	Quimionocicepción	Prostaglandina E2	Proteína Gs	Fosforilación de canales catiónicos
5HT-3	Quimionocicepción	Serotonina	Directo	Apertura de canales catiónicos
TNFR1	Quimionocicepción	TNF	P38/MAPK	Fosforilación de canales catiónicos
CXCR	Quimionocicepción	Quimiocinas	Proteína Gq	Desensibilización de receptores opioides

Los opioides y cannabinoides se acoplan a proteína Gi y eliminan el dolor al hiperpolarizar la célula activan do los canales de potasio y desactivar las proteínas gq y gs. Los aines bloquean las prostaglandinas

Finalmente entender que , así como el sistema inmune puede activar al nociceptor , el nociceptor también puede activar al sistema inmune.

El nociceptor puede mandar información via ortodrómica al cerebro , pero también antidrómica a la periferia. Y estando acoplado a fibras C amielínicas, estas fibras liberan en la periferia del nociceptor moléculas proinflamatorias que activan al macrófago.

Estas moléculas con el CGRP y las SUSTANCIA P, ESTAS MOLÉCULAS SE ACOPLAN A NUESTRO TEJIDO INMUNE Y NUESTRO ENDOTELIO.

LA ACTIVACIÓN DEL NOCICEPTOR causa que de manera directa el macrófago secrete factor de necrosis tumoral e interleucinas , damps y se genera una respuesta idéntica a como si hubiera daño tisular.

Cuando hay dolor neuropático el área se inflama (por la disfunción del nociceptor) dermalgia .

¿ Y ENTONCES APRENDÍ QUE ..?

- CUALQUIER ATRAPAMIENTO NEURAL O DOLOR NEUROPÁTICO PODÍAN RECLUTAR AL MACRÓFAGO Y GENERAR INFLAMACIÓN Y FIBROSIS.

Y ME ACORDÉ DE LA FASCIA , DE LA NEURODINÁMICA , DEL TRABAJO DEL OSTEÓPATA PARA DESACTIVAR AL MACRÓFAGO.

2.-IRRITACIÓN DEL NOCICEPTOR:

Así como el sistema inmune puede activar al nociceptor , el nociceptor también puede activar al sistema inmune.

¿ QUÉ MÁS SABEMOS?: ¿ QUÉ DICE LA EVIDENCIA CIENTÍFICA SOBRE LA MANIPULACIÓN OSTEOPÁTICA?.

- WALKOWSKI ET AL 2014

1.-MEJOR RESPUESTA INMUNE DE LOS INDIVIDUOS

2.-INCREMENTO DE LOS ANTICUERPOS Y REGULACIÓN DE LEUCOCITOS CIRCULANTES.

3.-MEJORA PERFIL INMUNOLÓGICO DE LOS INDIVIDUOS.

Leucocitos	5.746
Linfocitos	1.363
Linfocitos T	881
Linfocitos B	130
Linfocitos CD4+	231
Linfocitos CD8+	513
CD4/CD8	0.58
IgA	1.195
IgG	2.285
IgM	264

Walkowski S et al . Osteopathic manipulative therapy induces early plasma citoquine reléase and mobilization of a population of blood dendritic cells. PloS One 2014 Mar 10;9(3)e90132.

Algunos autores como Bialosky et al han propuesto en 2018 nuevos modelos neuroendocrinos en la aproximación a los efectos de la osteopatía

J Orthop Sports Phys Ther. 2018 Jan;48(1):8-18. doi: 10.2519/jospt.2018.7476. Epub 2017 Oct 15.

Unraveling the Mechanisms of Manual Therapy: Modeling an Approach.

Bialosky JE, Beneciuk JM, Bishop MD, Coronado RA, Penza CW, Simon CB, George SZ.

Abstract

Synopsis Manual therapy interventions are popular among individual health care providers and their patients; however, systematic reviews do not strongly support their effectiveness. Small treatment effect sizes of manual therapy interventions may result from a "one-size-fits-all" approach to treatment. Mechanistic-based treatment approaches to manual therapy offer an intriguing alternative for identifying patients likely to respond to manual therapy. However, the current lack of knowledge of the mechanisms through which manual therapy interventions inhibit pain limits such an approach. The nature of manual therapy interventions further confounds such an approach, as the related mechanisms are likely a complex interaction of factors related to the patient, the provider, and the environment in which the intervention occurs. Therefore, a model to guide both study design and the interpretation of findings is necessary. We have previously proposed a model suggesting that the mechanical force from a manual therapy intervention results in systemic neurophysiological responses leading to pain inhibition. In this clinical commentary, we provide a narrative appraisal of the model and recommendations to advance the study of manual therapy mechanisms. J Orthop Sports Phys Ther 2018;48(1):8-18. doi:10.2519/jospt.2018.7476.

KEYWORDS: manipulation; mobilization; neurophysiology; pain; theory

Comment in

May 2018 Letters to the Editor-in-Chief. [J Orthop Sports Phys Ther. 2018]

PMID: 29034802 DOI: 10.2519/jospt.2018.7476

Otros como Gyer et al se centran en los efectos corticales de la manipulación:

J Integr Med. 2019 May 9. pii: S2095-4964(19)30059-7. doi: 10.1016/j.joim.2019.05.004. [Epub ahead of print]

Spinal manipulation therapy: Is it all about the brain? A current review of the neurophysiological effects of manipulation.

Gyer G[1], Michael J[2], Inklebarger J[2], Tedla JS[3].

Author information

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2 The London College of Osteopathic Medicine, London NW1 6QH, United Kingdom.
3 Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, 3665 Guraiger, Abha, Saudi Arabia.

Abstract

Spinal manipulation has been an effective intervention for the management of various musculoskeletal disorders. However, the mechanisms underlying the pain modulatory effects of spinal manipulation remain elusive. Although both biomechanical and neurophysiological phenomena have been thought to play a role in the observed clinical effects of spinal manipulation, a growing number of recent studies have indicated peripheral, spinal and supraspinal mechanisms of manipulation and suggested that the improved clinical outcomes are largely of neurophysiological origin. In this article, we reviewed the relevance of various neurophysiological theories with respect to the findings of mechanistic studies that demonstrated neural responses following spinal manipulation. This article also discussed whether these neural responses are associated with the possible neurophysiological mechanisms of spinal manipulation. The body of literature reviewed herein suggested some clear neurophysiological changes following spinal manipulation, which include neural plastic changes, alteration in motor neuron excitability, increase in cortical drive and many more. However, the clinical relevance of these changes in relation to the mechanisms that underlie the effectiveness of spinal manipulation is still unclear. In addition, there were some major methodological flaws in many of the reviewed studies. Future mechanistic studies should have an appropriate study design and methodology and should plan for a long-term follow-up in order to determine the clinical significance of the neural responses evoked following spinal manipulation.

KEYWORDS: Complementary therapies; Occupational injuries; Occupational therapists; Physical therapists; Public health

PMID: 31105036 DOI: 10.1016/j.joim.2019.05.004

¿ QUÉ RESEÑAN LAS INVESTIGACIONES RECIENTES? Andrea Combi y Marco Testa

- Papel central que el Sistema neuroendocrino disfuncional puede jugar en el dolor musculoesquelético.
- Se han encontrado niveles elevados de citoquinas proinflamatoiras , TNF ALFA, INTERLEUKINA -1 ,6,8 en pacientes con espondiloartrosis.
- De hecho , se postula que las modificaciones estructurales que acontecen en las placas cartilaginosas terminales pueden ser la consecuencia del aumento de la infiltración de células inmunes y no solo resultado del envejecimiento.

Review

The Effects Induced by Spinal Manipulative Therapy on the Immune and Endocrine Systems

Andrea Colombi and Marco Testa *

Department of Neuroscience, Rehabilitation, Ophtalmology, Genetics, Maternal and Child Health, University of Genova, Campus of Savona, Via Magliotto, 2 17100 Savona, Italy

* Correspondence: marco.testa@unige.it

Received: 10 June 2019; Accepted: 2 August 2019; Published: 7 August 2019

Abstract: *Background and Objectives*: Spinal manipulations are interventions widely used by different healthcare professionals for the management of musculoskeletal (MSK) disorders. While previous theoretical principles focused predominantly on biomechanical accounts, recent models propose that the observed pain modulatory effects of this form of manual therapy may be the result of more complex mechanisms. It has been suggested that other phenomena like neurophysiological responses and the activation of the immune-endocrine system may explain variability in pain inhibition after the administration of spinal manipulative therapy (SMT). The aim of this paper is to provide an overview of the available evidence supporting the biological plausibility of high-velocity, low-amplitude thrust (HVLAT) on the immune-endocrine system. *Materials and Methods*: Narrative critical review. An electronic search on MEDLINE, ProQUEST, and Google Scholar followed by a hand and "snowballing" search were conducted to find relevant articles. Studies were included if they evaluated the effects of HVLAT on participants' biomarkers. *Results*: The electronic search retrieved 13 relevant articles and two themes of discussion were developed. Nine studies investigated the effects of SMT on cortisol levels and five of them were conducted on symptomatic populations. Four studies examined the effects of SMT on the immune system and all of them were conducted on healthy individuals. *Conclusions*: Although spinal manipulations seem to trigger the activation of the neuroimmunoendocrine system, the evidence supporting a biological account for the application of HVLAT in clinical practice is mixed and conflicting. Further research on subjects with spinal MSK conditions with larger sample sizes are needed to obtain more insights about the biological effects of spinal manipulative therapy.

Keywords: spinal manipulative therapy; immune system; endocrine system; back pain; neck pain; physiotherapy

Pain. 2014 Aug;155(8):1605-12. doi: 10.1016/j.pain.2014.05.007. Epub 2014 May 9.

Basal inflammation and innate immune response in chronic multisite musculoskeletal pain.

Generaal E[1], Vogelzangs N[2], Macfarlane GJ[3], Geenen R[4], Smit JH[2], Dekker J[5], Penninx BW[2].

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2 Department of Psychiatry and EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands.

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4 Department of Clinical and Health Psychology, Utrecht University, Utrecht, The Netherlands.

5 Department of Psychiatry and EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands; Department of Rehabilitation Medicine, VU University Medical Center, Amsterdam, The Netherlands.

Abstract

Dysregulation of the immune system may play a role in chronic pain, although study findings are inconsistent. This cross-sectional study examined whether basal inflammatory markers and the innate immune response are associated with the presence and severity of chronic multisite musculoskeletal pain. Data were used on 1632 subjects of the Netherlands Study of Depression and Anxiety. The Chronic Pain Grade questionnaire was used to determine the presence and severity of chronic multisite musculoskeletal pain. Subjects were categorized in a chronic multisite musculoskeletal pain group (n=754) and a control group (n=878). Blood levels of the basal inflammatory markers C-reactive protein, interleukin-6, and tumor necrosis factor-alpha were determined. To obtain a measure of the innate immune response, 13 inflammatory markers were assessed after lipopolysaccharide (LPS) stimulation in a subsample (n=707). Subjects with chronic multisite musculoskeletal pain showed elevated levels of basal inflammatory markers compared with controls, but statistical significance was lost after adjustment for lifestyle and disease variables. For some LPS-stimulated inflammatory markers, we did find elevated levels in subjects with chronic multisite musculoskeletal pain both before and after adjustment for covariates. Pain severity was not associated with inflammation within chronic pain subjects. An enhanced innate immune response in chronic multisite musculoskeletal pain may be examined as a potential biomarker for the onset or perpetuation of chronic pain.

KEYWORDS: C-reactive protein; Central sensitization; Chronic pain; Cytokines; Immune system; Innate immune response; Lipopolysaccharide

Clin Orthop Relat Res. 2015 Jun;473(6):1903-12. doi: 10.1007/s11999-014-3774-8.

Molecular basis of intervertebral disc degeneration and herniations: what are the important translational questions?

Kadow T[1], Sowa G, Vo N, Kang JD.

Author information

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Abstract

BACKGROUND: Intervertebral disc degeneration is a common condition with few inexpensive and effective modes of treatment, but current investigations seek to clarify the underlying process and offer new treatment options. It will be important for physicians to understand the molecular basis for the pathology and how it translates to developing clinical treatments for disc degeneration. In this review, we sought to summarize for clinicians what is known about the molecular processes that causes disc degeneration.

RESULTS: A healthy disc requires maintenance of a homeostatic environment, and when disrupted, a catabolic cascade of events occurs on a molecular level resulting in upregulation of proinflammatory cytokines, increased degradative enzymes, and a loss of matrix proteins. This promotes degenerative changes and occasional neurovascular ingrowth potentially contributing to the development of pain. Research demonstrates the molecular changes underlying the harmful effects of aging, smoking, and obesity seen clinically while demonstrating the variable influence of exercise. Finally, oral medications, supplements, biologic treatments, gene therapy, and stem cells hold great promise but require cautious application until their safety profiles are better outlined.

CONCLUSIONS: Intervertebral disc degeneration occurs where there is a loss of homeostatic balance with a predominantly catabolic metabolic profile. A basic understanding of the molecular changes occurring in the degenerating disc is important for practicing clinicians because it may help them to inform patients to alter lifestyle choices, identify beneficial or harmful supplements, or offer new biologic, genetic, or stem cell therapies.

PMID: 25024024 PMCID: PMC4418989 DOI: 10.1007/s11999-014-3774-8

[Indexed for MEDLINE] Free PMC Article

Acta Biochim Biophys Sin (Shanghai). 2017 Jan;49(1):1-13. doi: 10.1093/abbs/gmw112. Epub 2016 Nov 17.

Tumor necrosis factor-α: a key contributor to intervertebral disc degeneration.

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Author information

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EL TRATAMIENTO ANTI-TNF ALFA SE HA MOSTRADO PROMETEDORA PARA MITIGAR LA DEGENERACIÓN DISCAL.

Abstract

Intervertebral disc (IVD) degeneration (IDD) is the most common cause leading to low back pain (LBP), which is a highly prevalent, costly, and crippling condition worldwide. Current treatments for IDD are limited to treat the symptoms and do not target the pathophysiology. Tumor necrosis factor-α (TNF-α) is one of the most potent pro-inflammatory cytokines and signals through its receptors TNFR1 and TNFR2. TNF-α is highly expressed in degenerative IVD tissues, and it is deeply involved in multiple pathological processes of disc degeneration, including matrix destruction, inflammatory responses, apoptosis, autophagy, and cell proliferation. Importantly, anti-TNF-α therapy has shown promise for mitigating disc degeneration and relieving LBP. In this review, following a brief description of TNF-α signal transduction, we mainly focus on the expression pattern and roles of TNF-α in IDD, and summarize the emerging progress regarding its inhibition as a promising biological therapeutic approach to disc degeneration and associated LBP. A better understanding will help to develop novel TNF-α-centered therapeutic interventions for degenerative disc disease.

KEYWORDS: ECM; IDD; TNF-α; TNFR1; TNFR2

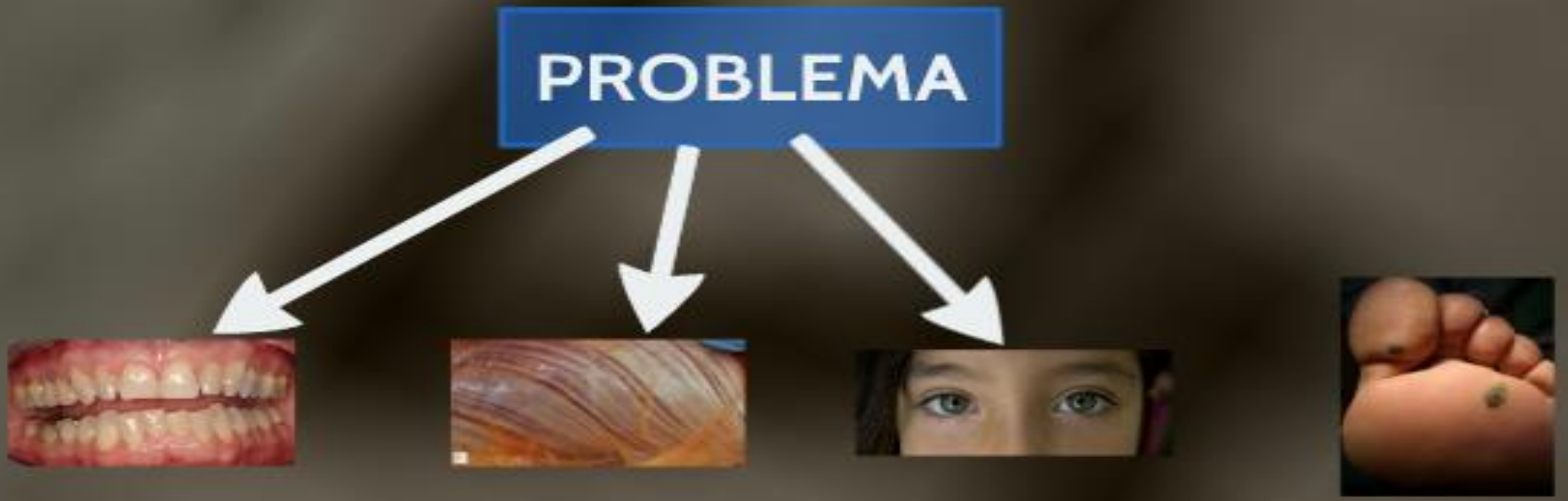
PMID: 27864283 DOI: 10.1093/abbs/gmw112

EL DOLOR:

- La Asociación Internacional para el Estudio del Dolor definió el dolor como "una experiencia sensitiva y emocional desagradable, asociada a una lesión tisular real o potencial"

Cuando llega un paciente a vuestra consulta con una contractura o un esguince de tobillo , soléis hacer tratamientos a nivel local.

La mayoría de las recidivas son consecuencia de problemas situados a distancia.

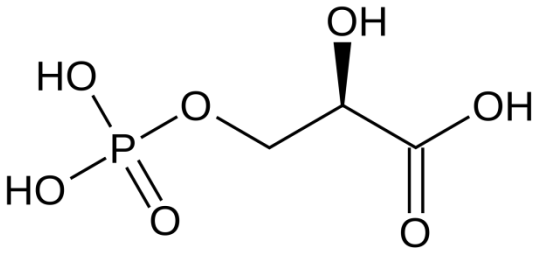


4.- PROCEDENCIA DEL DOLOR EN LAS LESIONES DEL TEJIDO CONECTIVO

3 fosfoglicerato :

Residuo derivado de la

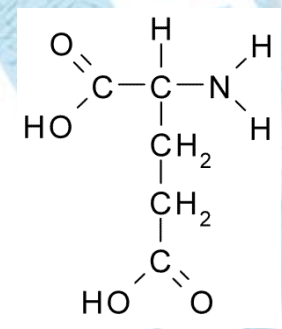
glucosa en el ciclo de Krebs

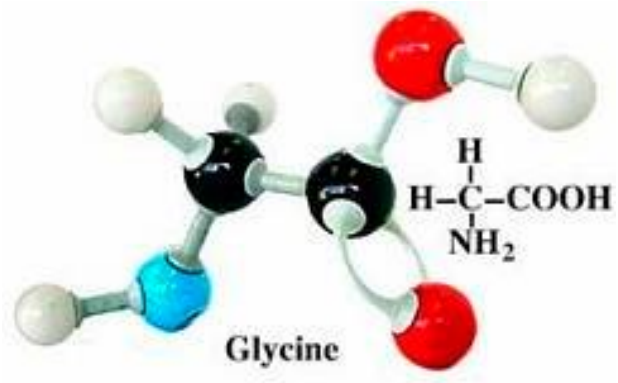


Coenzima nicotin adenin dinucleótido fosfato.

Transferencia de electroens y protones .

Reducción: NAD+ A NADH





GLUTAMATO : aminoácido excitador por excelencia

en cerebro y nocicepción tendón.

Por mediación del cetoglutarato pasa a FOSOFOGLICERAMONIO y mediante la fosfoserín fosfatasa pasa a SERINA que mediante la serina hidroxietil-transferasa pasa a GLICINA.

- El glutamato, uno de los neurotransmisores más abundantes en el sistema nervioso (se supone que es liberado en más de la mitad de las sinapsis del sistema nervioso),realiza su acción excitadora actuando sobre receptores específicos localizados en la membrana neuronal.

- Los receptores ionotrópicos de glutamato se denominan según la molécula agonista que los activa: los receptores NMDA, por el N-metil-D-aspartato, los receptores de tipo AMPA, por a-amino-3-hidroxil-5-metil-4- isoxazol-propionato y los receptores de tipo kainato, por el ácido kaínico. Estos tres tipos de receptores forman canales catiónicos no selectivos, permeables tanto para el Na+ como para el K+, de manera que la unión del glutamato sobre cualquiera de ellos provoca una despolarización de la membrana postsináptica (un potencial excitador postsináptico o EPSP).

El canal formado por el receptor NMDA permite el paso de los iones Ca2+, además del Na+ y K+, lo que implica un incremento de la concentración de Ca2+ intracelular en la neurona postsináptica cada vez que el receptor se activa.

Para que el canal se abra se necesita, además del glutamato, la presencia de un co-agonista (el aminoácido glicina). Ciertas poliaminas, al igual que la glicina, modulan positivamente el canal,mientras que el cinc, el magnesio y un exceso de protones lo modulan negativamente.

- ¿ QUÉ CONSECUENCIAS TIENEN ESTAS REACCIONES QUÍMICAS?

SI QUEREMOS REDUCIR LA SENSIBILIZACIÓN CENTRAL Y PERIFÉRICA.

SI QUEREMOS REGENERAR TENDONES .

DEBEMOS ADMINISTRAR MAGNESIO, ZINC, GLICINA Y LISINA (PISTACHOS).

EL MAGNESIO Y EL ZINC VAN A REDUCIR LOS ESTÍMULOS EXCITADORES VÍA RECEPTOR NMDA.

LA GLICINA Y LISINA INDUCIR LA REPARACIÓN TENDINOSA.

De dónde proviene el dolor:

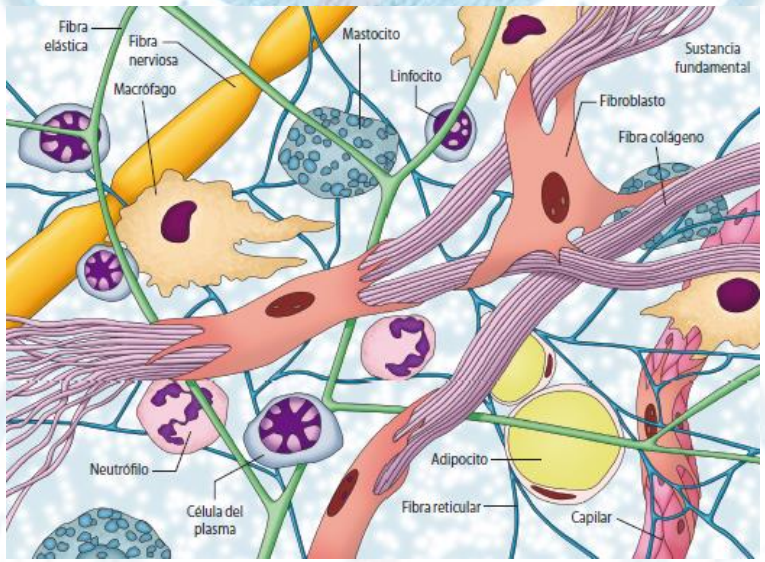
- El glutamato , un conocido neurotransmisor y un potente modulador del dolor en el sistema nervioso central , se encuentra en grandes cantidades en las estructuras del tejido conectivo dolorosas y no así en las asintomáticas. Por ello la dieta y la actividad aeróbica son necesarias para la recuperación.

- Parece ser que algunas de **las vías neurógenas desencadenantes del dolor están relacionadas con la angiogénesis-asocida a neurogénesis**. Por ello, la escleroterapia es una buena opción.

- **Algunos estudios muestran que la sustancia P está presente en la pared de estos neovasos por lo que la electroterapia analgésica es interesante.**

- **Calcitonin gene-related peptide está tb presente por lo que se impone también la realización de ejercicios repetitivos con poco peso y trabajo fascial para desactivarlo.**

Fascia y Matriz Extracelular.



Reactive tendinopathy

Type of tendinopathy	Reactive/ Proliferative	Dysrepair/ Failed healing	Degenerative
Tendon response	Active Adapting to (over)load	Active Attempting to heal	Passive – 'burnt out' Gives up on healing
Tendon	Increased GAG & protein production	Continues protein production but fails to gain structure	Cells die, no protein production
Age/load	Younger (15-25 yrs) short term overload	Older (20-35yrs) and/or subject to ongoing high load	Oldest (30-60 yrs) and/or subject to further strain
Capacity to repair	Full – given optimal conditions	Limited	None - can progress to rupture
Prevalence	Less common	More common	Common
Pain ??????	Yes - ? threshold	Sometimes	Variable

PROCEDENCIA DEL DOLOR (GENERALIDADES)

DIFERENTES NOXAS INDUCEN DAÑO TISULAR Y DESPOLARIZACIÓN DE NOCICEPTORES:

- POTASIO,sustancias algógenas prostaglandinas,leucotrienos: liberado por las células dañadas.
- SEROTONINA: liberado por las plaquetas.
- Bradiquinina: en plasma.
- Histamina : liberada por los mastocitos.
- Sustancia P y cgrp: liberados por las fibras aferentes primarias.

Todas estas inducen despolarización de receptores y transmisión a centros superiores.

Thomas J, Klingler W. The influence of pH and other metabolic actors on fascial properties. In: Schleip R, Findley TW, Chaitow L, Huijing PA (Eds.). Fascia: the Tensional Network of the Human Body. Churchill Livingstone Elsevier: Edinburgh. 2012. pp. 171/176.

Los cambios en el pH, el contenido iónico y la temperatura pueden representar factores ambientales y metabólicos claves que influyen en la viscosidad fascial (Thomas y Klingler, 2012).

Ohshima H, Urban JP. The effect of lactate and pH on proteoglycan and protein synthesis rates in the intervertebral disc. Spine (Phila Pa 1976). 1992 Sep; 17(9):1079-82.
Levick JR. Hypoxia and acidosis in chronic inflammatory arthritis; relation to vascular supply and dynamic effusion pressure. J Rheumatol. 1990 May; 17(5):579-82.
Mwale F, Ciobanu I, Giannitsios D, Roughley P, Steffen T, Antoniou J. Effect of oxygen levels on proteoglycan synthesis by intervertebral disc cells. Spine (Phila Pa 1976). 2011 Jan 15; 36(2):E131-8.

Un ambiente ácido de la matriz extracelular parece ejercer una acción de modulación en el metabolismo y la síntesis de la proteína de las células del tejido conectivo, tales como fibroblastos y condrocitos (Ohshima y Urbano, 1992).

Es responsable de una predisposición a reacciones inflamatorias y a daño tisular durante estos altos niveles de acidosis (Levick, 1990); existe un deterioro de la remodelación y reparación de los tejidos con un pH inferior a 6,5 (van den Berg); y produce efectos benéficos sobre la composición de la matriz gelatinosa y fibrosa (Mwale et al., 2011).

Spine (Phila Pa 1976). 1992 Sep;17(9):1079-82.

The effect of lactate and pH on proteoglycan and protein synthesis rates in the intervertebral disc.

Ohshima H[1], Urban JP.

Author information

EL METABOLISMO DISCAL ES ANAEROBIO , EL LACTATO PRODUCIDO ES 8-10 VECES EL PLASMÁTICO. LA CAÍDA DE LOS NIVELES DE O2 COMO RESULTADO , POR EJEMPLO DEL TABACO LLEVAN A UNA CAÍDA EN LA SÍNTESIS DE PROTEOGLICANOS Y A DEGENERACIÓN DISCAL.

Abstract

The intervertebral disc is the largest avascular tissue in the body. Its metabolism is mainly anaerobic, and thus lactate is produced at a significant rate. As a result the lactate concentrations in the center of the disc may be 8-10 times as high as in the plasma. The pH in the disc center is thus acidic. Because low values of pH are known to affect proteoglycan synthesis in other cartilages, the authors measured the effect of lactate levels and pH on 35S-sulphate and 3H-proline incorporation rates in the nucleus of bovine coccygeal discs and in human disc obtained during percutaneous nucleotomy. The maximum incorporation rate occurred at pH 7.2-pH 6.9. Here the rate was 40-50% greater than at pH 7.4. Below pH 6.8 the rate fell steeply, more so for sulphate than for proline. At pH 6.3 the sulphate incorporation rate was around 20 percent that at pH 7.4. The results indicate that proteoglycan synthesis rates in particular are sensitive to extracellular pH, and that the peak rate occurs around the level of pH seen in vivo. Factors that cause lactate levels to rise, such as a fall in O2 levels as the result of smoking or vibration (Holm and Nachemson, 1988) could lead to a fall in proteoglycan synthesis rates, ultimately leading to a fall in proteoglycan content and to disc degeneration.

PMID: 1411761

Spine (Phila Pa 1976). 2011 Jan 15;36(2):E131-8. doi: 10.1097/BRS.0b013e3181d52b9e.

Effect of oxygen levels on proteoglycan synthesis by intervertebral disc cells.

Mwale F[1], Ciobanu I, Giannitsios D, Roughley P, Steffen T, Antoniou J.

Author information

ARTÍCULO QUE AFIRMA LO CONTRARIO QUE EL ANTERIOR

Abstract

STUDY DESIGN: the response of cells from the annulus fibrosus (AF) and nucleus pulposus (NP) to varying oxygen (O2) concentrations was examined when cultured in alginate.

OBJECTIVE: to study the effect of O2 concentration on AF and NP cells.

SUMMARY OF BACKGROUND DATA: AF and NP cells possess different metabolic profiles in situ. However, it is not clear whether this difference is maintained in in vitro culture conditions. AF and NP cells can respond differently in the different systems, which may differ from the in vivo environment in terms of nutrient supply and O2 levels. In vivo, O2 levels vary from 1% to 5% within the intervertebral disc, and there is evidence that disc cell metabolism can vary with O2 concentrations.

METHODS: an alginate scaffold was seeded with bovine AF or NP cells and maintained in culture for up to 18 days under different O2 concentrations. The sulfated glycosaminoglycan (GAG) content in the culture medium and the expression of aggrecan, type I (COL1A2) and II (COL2A1) collagen genes were analyzed at day 9 and day 18.

RESULTS: in both NP and AF cells cultured either in normoxia (21% O2) or in hypoxia (5% and 1% O2), the GAG content of the culture medium increased with time, though the rate of increase was diminished in 5% O2. With a decrease in O2 levels, the expression of aggrecan mRNA increased in NP cells. There was little effect of O2 on aggrecan mRNA level in AF cells. However, there was a slight decrease with time. Interestingly, aggrecan mRNA levels did not reflect GAG release for either NP or AF cells. There was no effect with time or O2 levels on COL2A1 message in NP cells. The highest Aggrecan/COL2 message ratio for NP cells was with 1% O2, suggesting this to be the best condition for maintaining the NP phenotype. COL1A2 gene expression in NP and AF cells increased with time, but showed little change with O2 levels in NP cells. The highest COL2/COL1 ratio in NP cells was also observed with 1% O2. Finally, NP cells tended to remain localized in the alginate beads, whereas AF cells tended to migrate from the beads.

CONCLUSION: both NP and AF cells showed little change in GAG production with O2 levels ranging from 1% to 21%. Disc cell metabolism is not impaired at low O2 concentrations, which appear beneficial to matrix composition. Furthermore, low oxygen may promote a gelatinous NP matrix, whereas increased oxygen levels may promote a fibrous matrix.

PMID: 21057384 DOI: 10.1097/BRS.0b013e3181d52b9e

J Rheumatol. 1990 May;17(5):579-82.

Hypoxia and acidosis in chronic inflammatory arthritis; relation to vascular supply and dynamic effusion pressure.

Levick JR[1].

Author information

UNA ARTICULACIÓN CRÓNICAMENTE INFLAMADA ES HIPÓXICA Y ACIDÓTICA. UNA SINOVIAL ENGROSADA REDUCE SU DENSIDAD CAPILAR Y , POR ENDE, EL FLUJO VASCULAR.

Abstract

The chronically inflamed joint is usually chronically hypoxic and acidotic, and this is due partly to a high synovial metabolic rate, partly to reduced synovial capillary density and capillary "burial" under thickened synovium, and partly, in the end stages, to a chronically reduced blood flow. In addition, recent work indicates that prolonged flexion or strong muscular contraction around a chronically inflamed joint (knee) can exacerbate the biochemical abnormalities, by transiently raising intraarticular pressure to such high levels as to further impair synovial blood flow. The resulting unphysiological internal environment is presumably detrimental per se to the joint's well being, though precisely how requires more explicit investigation. The possibility that the subsequent reperfusion during joint relaxation is itself a damaging, radical generating process represents an additional exciting, albeit still contentious development.

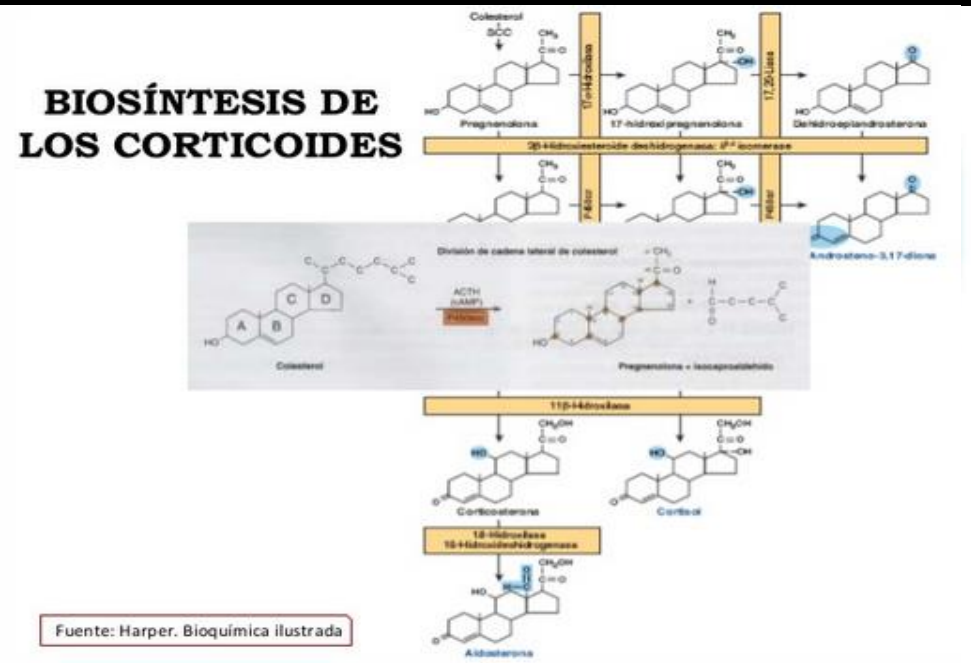
PMID: 2359066

¿qué OFRECE LA OSTEOPATÍA? *Tomado de F. Ricard.*

- Que la manipulación vertebral genera hipoalgesia, actúa sobre el sistema nervioso actuando sobre los receptores propioceptivos paravertebrales , elimina aferencias aberrantes (George et al 2006, Pickar 2002), reduce la magnitud de los potenciales cerebrales evocados (Zhu et al 2000) , estimula la circunvolución prerrolándica (Meier et al) modificando la plasticidad cortical.
- Trabajando sobre sensibilización central y periférica.

Benarroch EE. Pain-autonomic interactions. Neurol Sci. 2006 May; 27 Suppl 2:S130-3. Review.
Peyron R, Laurent B, García-Larrea L. Functional imaging of brain responses to pain. A review and meta-analysis (2000). Neurophysiol Clin. 2000 Oct; 30(5):263-88.

NEUROENDOCRINOLOGÍA DE LA PIEL: Michal A. Zmijewski1 and Andrzej T. Slominski 2018.



Neuroendocrinology of the skin An overview and selective analysis Michal A. Zmijewski1 and
Andrzej T. Slominski2,* 1Department of Histology; Medical University of Gdansk; Gdansk,
Poland; 2Department of Pathology and Laboratory Medicine; Center for Cancer Research;University of Tennessee Health Science Center; Memphis, TN USA

Dermatoendocrinol. 2011 Jan;3(1):3-10. doi: 10.4161/derm.3.1.14617.

Neuroendocrinology of the skin: An overview and selective analysis.

Zmijewski MA[1], Slominski AT.

Author information

Abstract

The concept on the skin neuro-endocrine has been formulated ten years ago, and recent advances in the field further strengthened this role. Thus, skin forms a bidirectional platform for a signal exchange with other peripheral organs, endocrine and immune systems or brain to enable rapid and selective responses to the environment in order to maintain local and systemic homeostasis. In this context, it is not surprising that the function of the skin is tightly regulated by systemic neuro-endocrine system. Skin cells and skin appendages not only respond to neuropeptides, steroids and other regulatory signals, but also actively synthesis variety of hormones. The stress responses within the skin are tightly regulated by locally synthesized factors and their receptor expression. There is growing evidence for alternative splicing playing an important role in stress signaling. Deregulation of the skin neuro-endocrine signaling can lead or/and be a marker of variety of skin diseases. The major problem in this area relates to their detailed mechanisms of crosstalk between skin and brain and between the local and global endocrine as well as immune systems.

KEYWORDS: POMC; corticotropin releasing factor (CRF); homeostasis; hormones; melatonin; neurotransmitters; regulatory network; skin; stress

PMID: 21519402 PMCID: PMC3051846 DOI: 10.4161/derm.3.1.14617

AMPLIAR EL CAMPO DE INVESTIGACIÓN

- **NUEVAS TESIS** QUE SE CENTREN POR EJEMPLO **EN CÓMO EL TRATAMIENTO FASCIAL AFECTA A LA ESTEROIDOGÉNESIS EN LA PIEL.**