Tesis doctoral bajo el título

APROXIMACIÓN A LA HIPÓTESIS DE UN DÉFICIT SENSORIOMOTOR EN LA PARÁLISIS CEREBRAL

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A todos los que me han ayudado todos estos años.

A todos los que, a pesar de todo, todavía siguen conmigo.

A los chicos, familias y profesionales que después de todo este tiempo ya me conocen como "la chica del dolor".

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Resumen

La parálisis cerebral se ha considerado clásicamente como un trastorno motor, donde las alteraciones de la sensibilidad somatosensorial han sido escasamente consideradas. Esta investigación pretende explorar la hipótesis de que las personas con parálisis cerebral presenten déficits sensoriomotores. Para ello, se han llevado a cabo diversos estudios para explorar el procesamiento somatosensorial de los pacientes con parálisis cerebral y voluntarios sanos. Además de un estudio sociodemográfico sobre la incidencia del dolor y los déficits somatosensoriales en esta población, se presentan datos sobre los umbrales sensoriales ante el tacto y la presión, así como sobre la actividad cerebral desencadenada por la estimulación mecánica y el movimiento de diferentes partes del cuerpo. Finalmente, se llevó a cabo un programa de intervención terapéutica en la que se intentaron aplicar los conocimientos adquiridos en los estudios previos. Los resultados de la presente investigación confirmaron que las personas con parálisis cerebral padecen mayor dolor y déficits somatosensoriales en comparación con los voluntarios sanos. Además, se observó que el procesamiento de la información somatosensorial presentaba una asimetría hemisférica dependiente de la afectación motriz. Por otra parte, el procesamiento motor presentó alteraciones significativas que estaban relacionadas, fundamentalmente, con el periodo de planificación motora, donde las aferencias sensoriales son de capital importancia. Estos datos apoyan la hipótesis de la existencia de un déficit sensoriomotor y subrayan la necesidad de implementar la valoración y el tratamiento específico de los déficits somatosensoriales en las personas con parálisis cerebral.

I

Introducción

La parálisis cerebral ha sido considerada tradicionalmente como un trastorno motor. Esta concepción ha marcado la investigación y la actuación clínica ante la patología, donde la valoración y el tratamiento de aspectos motores como el tono muscular, los problemas ortopédicos, la postura y el movimiento han prevalecido sobre la valoración y el tratamiento de otros trastornos, como el dolor y los déficits somatosensoriales (Rosembaum et al., 2007). La presente investigación pretende profundizar en la idea de que la parálisis cerebral, además de un trastorno motor, es una patología que presenta graves problemas en el procesamiento somatosensorial que pueden, a su vez, afectar a la función motora de estos sujetos.

En las últimas dos décadas, se ha demostrado repetidamente que los mapas somatotópicos que permiten las funciones sensoriales y motoras pueden cambiar en respuesta a la experiencia, particularmente durante el desarrollo pero también en la edad adulta (Tycs & Boyadjian, 2011; Bleton et al., 2010; Wittenberg, 2009). También se ha sugerido que la anormal percepción somatosensorial producida por la patología desde edades tempranas podría, de forma potencial, causar cambios a largo plazo en el procesamiento de la información sensitiva y dolorosa (Schmelzle-Lubiecki et al., 2007). Esto hace que el estudio de la relación entre los déficits sensoriales y motores en personas con daño cerebral temprano, sea un campo propicio para el estudio de la plasticidad cerebral y pueda tener aplicaciones clínicas para mejorar las estrategias de rehabilitación.

Esta investigación pretende estudiar el déficit somatosensorial en la parálisis cerebral desde tres perspectivas: 1) conocer las diferencias que puedan existir entre las personas con parálisis cerebral y la población sana; 2) determinar si existen diferencias debidas a la edad, y 3) analizar las diferencias que puedan existir entre personas con parálisis cerebral de distinta afectación motora. Para ello, la investigación se ha centrado en dos parámetros fundamentales: la sensibilidad táctil, fuente esencial de las aferencias para las acciones motoras y el dolor, un problema secundario importante en las personas con parálisis cerebral e íntimamente asociado con la sensibilidad táctil.

En la investigación se evalúan diferentes aspectos del procesamiento somatosensorial y su relación con la afectación motora en distintos niveles funcionales: abordando los aspectos sociodemográficos mediante cuestionarios, analizando los mecanismos fisiológicos que lo regulan mediante técnicas psicofisiológicas y de registro de la

actividad cerebral y valorando los cambios en los parámetros somatosensoriales que se producen como consecuencia de una intervención terapéutica.

1.1. La parálisis cerebral

La *American Academy for Cerebral Palsy and Developmental Medicine* (AACPDM) define la parálisis cerebral como un grupo de trastornos del desarrollo del movimiento y la postura, que limitan la actividad, y que se atribuyen a trastornos no progresivos que ocurren en el cerebro en desarrollo del feto o del niño pequeño. La AACPDM señaló que los problemas motores de la parálisis cerebral se acompañan frecuentemente de trastornos de la sensibilidad, cognición, comunicación, percepción, comportamiento y/o crisis epilépticas (Bax et al., 2005).

En cuanto a la prevalencia, la parálisis cerebral constituye la discapacidad física infantil más común. Afecta a 2-2,5 niños por cada 1.000 nacimientos y puede producirse por daño cerebral ocurrido en el periodo prenatal (70-80% de los casos), durante el nacimiento (asfixia durante el parto, 6% de los casos) o después del nacimiento, hasta el fin de la maduración del SNC (10-20% de los casos), debido a procesos como meningitis bacteriana, encefalitis viral, hiperbilirrubenia o traumatismos, entre otros. Existen factores de riesgo que permiten un seguimiento y detección temprana de la patología, como la prematuridad, peso en el nacimiento inferior a 1.500 g., retraso en el crecimiento intrauterino, hemorragia intracraneal, hábitos tóxicos de la madre durante el embarazo, etc. (Krigger, 2006).

El diagnóstico se realiza por observación del retraso en el desarrollo motor del lactante, tono muscular anormal, posturas inusuales y persistencia de los reflejos primitivos más allá de su periodo de permanencia, así como la alteración en su presentación. Las técnicas de neuroimagen, como la resonancia magnética nuclear y la tomografía computerizada, ayudan a completar el diagnóstico.

La AACPDM sugirió que los distintos trastornos agrupados bajo el paraguas de la definición de parálisis cerebral, se clasificaran según distintos criterios:

Tabla I. Componentes de la clasificación de la parálisis cerebral (AACPDM, 2005).

1. Trastornos motores	a) Naturaleza y tipología del trastorno motor	Anormalidades del tono Desórdenes del movimiento: espasticidad, ataxia, distonía o atetosis.
	b) Capacidad funcional	Limitación de la función motora.
2. Trastornos asociados	Presencia o ausencia de problemas no motrices	Trastornos sensoriales, crisis epilépticas, déficits de atención, comportamiento, comunicación o cognitivos.
	Grado en el que estos problemas interaccionan	
3. Signos anatómicos y radiológicos	a) Distribución anatómica	Partes del cuerpo (miembros, tronco) afectadas.
	b) Hallazgos radiológicos	Anormalidades corticales, elongación ventricular, pérdida de sustancia blanca…
4. Etiología y cronología	Causa clara identificada	Ej. Meningitis, traumatismo, malformaciones…
	Ventana temporal durante la que ocurrió el daño cerebral	

En nuestro trabajo utilizaremos la clasificación adoptada por la *Surveillance of Cerebral Palsy in Europe* (SCPE), (2000) para agrupar a nuestros sujetos experimentales (Figuras 1 y 2). La SCPE es una red europea que agrupa los registros de 25 centros de 11 países para realizar estudios epidemiológicos sobre la parálisis cerebral. La validez de estos criterios para la clasificación de los sujetos con parálisis cerebral se han demostrado en estudios posteriores (Gainsborough et al., 2008).
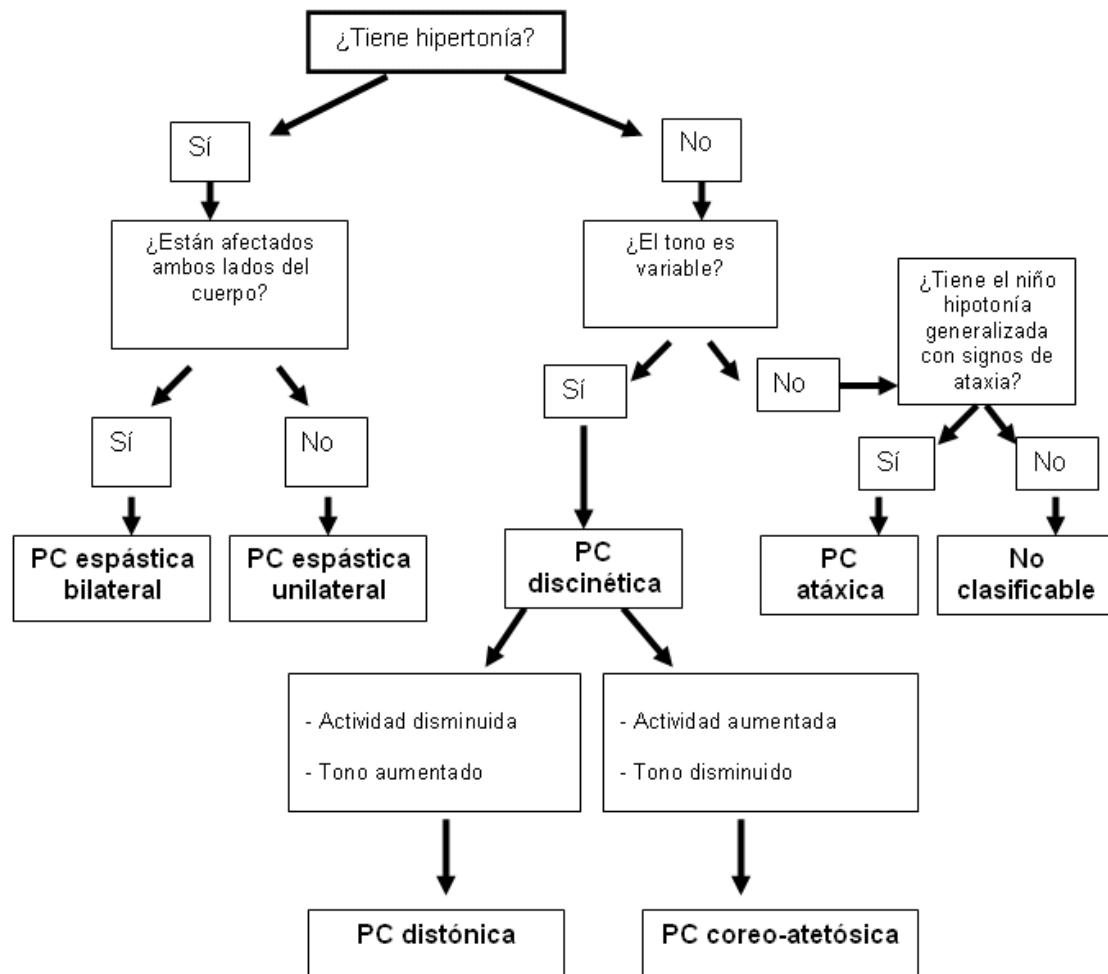
Figura 1. Árbol de clasificación de la parálisis cerebral. Surveillance of Cerebral Palsy in Europe (SCPE), 2000.

Como puede observarse en la Figura 1, los principales criterios para la clasificación de las personas con parálisis cerebral son las distintas alteraciones del tono muscular. Así, la presencia de hipertonía, hipotonía o de un tono variable, determina los principales subtipos de parálisis cerebral. Otros factores que permiten completar la clasificación son la presencia de ataxia, la intensidad de la actividad y la afectación de uno o ambos hemicuerpos.

En base a dicho criterio, la Figura 2 muestra datos epidemiológicos sobre la prevalencia, signos clínicos, principales zonas del SNC afectadas y postura típica de cada uno de los subtipos de parálisis cerebral.

Tipología de parálisis cerebral

Espástica (80%)

Hipertonía.
Hiperreflexia y/o
signos piramidales.

Discinética (10-20%)

Movimientos involuntarios,
incontrolados, recurrentes,
estereotipados.

Atáxica (5-10%)

Falta de coordinación muscular.
Los movimientos se realizan
con fuerza, ritmo y destreza
anormal.
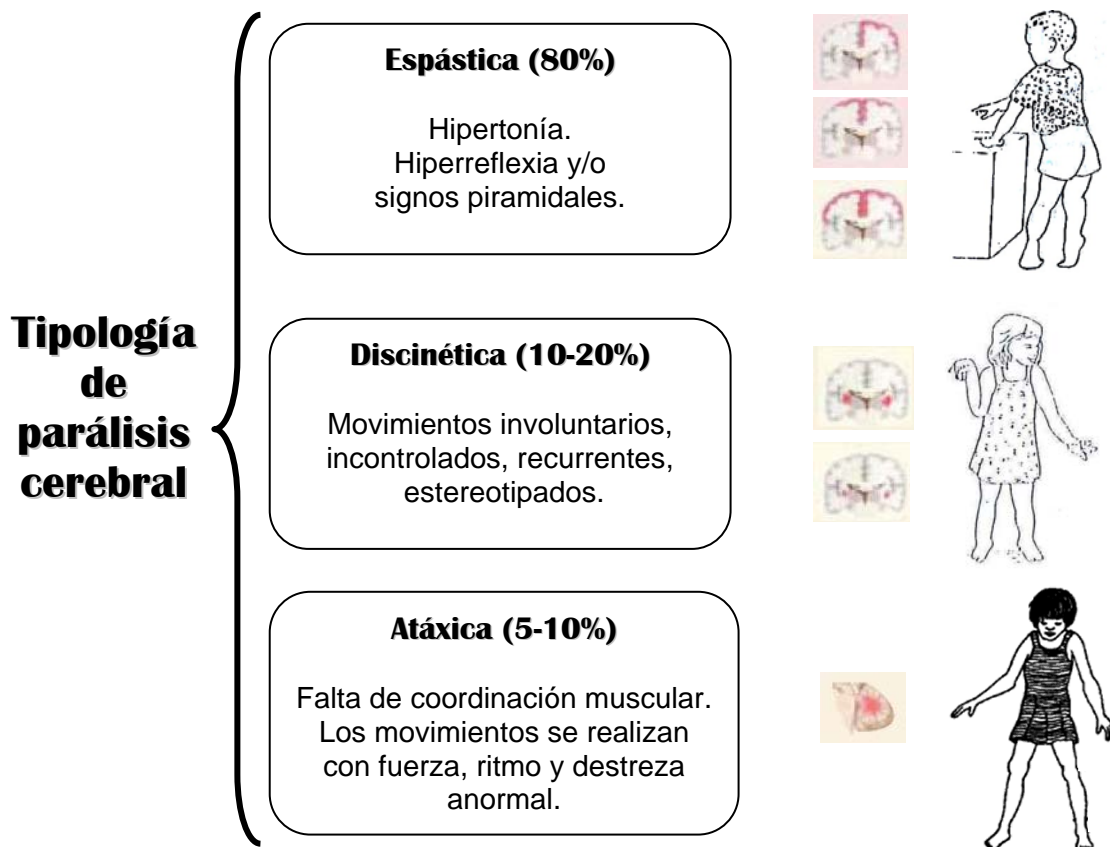
Figura 2. Clasificación de la parálisis cerebral según la tipología del trastorno motor. Surveillance of Cerebral Palsy in Europe (SCPE), 2000.

Dado que el trastorno es eminentemente motor, se utilizan diversas herramientas de evaluación motriz (escalas para la medición de la espasticidad, de función motora gruesa, manipulación y otras escalas funcionales) no sólo para clasificar a las personas con parálisis cerebral según su grado de afectación motora, sino también para evaluar su evolución a lo largo del tiempo o como resultado del tratamiento. La Tabla II presenta un breve resumen de las herramientas de evaluación más utilizadas.

Tabla II. Herramientas de valoración de la función motora. Fuente: Sociedad española de fisioterapia en pediatría (SEFIP).

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Valoración de la funcionalidad y autonomía	*ASSESSMENT, EVALUATION, AND PROGRAMMING SYSTEM FOR INFANTS AND CHILDREN (AEPS)*	0-18 meses
	FUNCTIONAL OUTCOMES ASSESSMENT GRID (FOAG)	6 meses-8 años
	FUNCTIONAL INDEPENDENCE MEASURE FOR CHILDREN (WeeFIM)	+ 7 años
	FUNCTIONAL INDEPENDENCE MEASURE (FIM)	
	PEDIATRIC EVALUATION OF DISABILITY INVENTORY (PEDI)	6 meses- 7 años
	SCALES OF INDEPENDENT BEHAVIOR-REVISED (SIB-R)	+ 3 meses
Valoración de función motora gruesa	*ALBERTA INFANT MOTOR SCALE (AIMS)*	0-18 meses
	GROSS MOTOR FUNCTION MEASURE (GMFM)	5 meses- 16 años
	MILANI-COMPARETTI MOTOR DEVELOPMENT SCREENING TEST	0-2 años
	MEADE MOVEMENT CHECKLIST (MMCL)	4-6 meses
	TEST OF INFANT MOTOR PERFORMANCE (TIMP)	34 semanas de gestación-4 meses
	TODDLER & INFANT MOTOR EVALUATION (TIME)	4-42 meses
Valoración de función motora fina	*QUALITY OF UPPER EXTREMITY TEST (QUEST)*	
	MANUAL ABILITY CLASSIFICATION SYSTEM (MACS)	4-18 años
Valoración de desarrollo psicomotor	*AGES & STAGES QUESTIONNAIRES (ASQ)*	4-60 meses
	BATTELLE DEVELOPMENTAL INVENTORY (BDI)	0-8 años
	BAYLEY SCALES OF INFANT DEVELOPMENT-II	0-42 meses
	DENVER-II	0-2 años
	EARLY INTERVENTION DEVELOPMENTAL PROFILE (EDP)	0-3 años
	REVISED GESELL AND AMATRUDA DEVELOPMENTAL AND NEUROLOGIC EXAMINATION	1-36 meses
	INFANT TODDLER DEVELOPMENTAL ASSESSMENT (IDA)-PROVENCE PROFILE	0-3 años
	INFANT MOTOR SCREEN (IMS)	4-16 meses de edad corregida
	PEABODY DEVELOPMENTAL MOTOR SCALES	1-82 meses
Valoración del equilibrio	BERG BALANCE TEST	+5 años
	FUNCTIONAL REACH TEST (FRT)	+ 4 años
	PEDIATRIC CLINICAL TEST OF SENSORY INTERACTION FOR BALANCE (P-CTSIB)	4-10 años
Valoración de la marcha	*NINE MINUTE WALK TEST*	+ 5 años
	OBSERVATIONAL GAIT SCALE (OGS)	6-20 años
	TIMED OBSTACLE AMBULATION TEST (TOAT)	
	TIMED UP AND GO (TUG)	+ 4 años
Valoración del tono muscular	*MODIFIED ASHWORTH SCALE* (MAS)	+ 4 años
Valoración musculoesquelética	LEG LENGTH DISCREPANCY TAPE MEASURE	
	MANUAL MUSCLE TEST (MMT)	+ 4 años
	TEST FOR HIP JOINT INTEGRITY	

En el presente trabajo hemos utilizado el Gross Motor Function Classification System (GMFCS) (Palisano et al., 1997), un sistema de clasificación de la parálisis cerebral desarrollado a partir del GMFM, que clasifica a las personas con parálisis cerebral según las destrezas exhibidas en la función motora gruesa y el desplazamiento en cada edad. El GMFCS es el sistema de clasificación motora más aceptado a nivel internacional y ha sido utilizado ampliamente como método de clasificación en la mayoría de los trabajos científicos sobre el tema. El GMFCS es un sistema de clasificación en 5 niveles, basado en la función, la movilidad en espacios interiores y exteriores y la necesidad de ayudas técnicas o tecnológicas que asistan en la movilidad (caminadores, muletas, bastones y sillas de ruedas) de los individuos. Aunque está desarrollada principalmente para la edad infantil, hemos considerado que podía sea interesante aplicarla también en nuestra muestra de población adulta con parálisis cerebral, ya que proporciona una idea bastante precisa del grado de afectación motora gruesa que padecen estas personas. La Figura 3 recoge de forma resumida los criterios para la clasificación en los distintos niveles del sistema GMFCS.

Nivel I GMFCS: Camina sin limitaciones.

- Camina en el interior o exterior, sube escaleras sin limitaciones.
- Realiza actividades motoras gruesas que incluyen correr y saltar, pero la velocidad, equilibrio y coordinación están alterados.
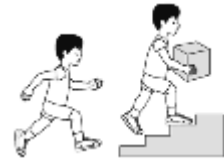
Nivel II GMFCS: Camina con limitaciones.

- Presenta limitaciones para realizar actividades en el exterior.
- Camina en el interior y exterior y sube escaleras agarrado del pasamanos, tiene limitación para caminar en superficies accidentadas o inclinadas y para caminar entre multitudes.
- Mínima capacidad para correr y saltar.
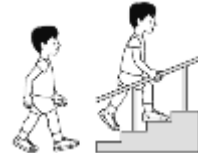
Nivel III GMFCS: Camina con ayudas técnicas.

- Camina en exterior o interior sobre superficies planas con ayuda de un aparato.
- Puede ser capaz de subir escaleras agarrado del pasamanos.
- Puede impulsar una silla de ruedas manualmente pero necesitan ayuda en las distancias largas en el exterior o en terreno accidentado.

Nivel IV GMFCS: Movilidad con limitaciones. Puede utilizar silla de ruedas eléctrica.

- Movilidad autónoma limitada severamente, incluso con ayudas técnicas.
- Utilización de silla de ruedas la mayor parte del tiempo. Puede autopropulsar la silla de ruedas.

Nivel V GMFCS: Transportado con silla de ruedas.

- Deficiencias físicas que restringen el control del movimiento voluntario y la capacidad de mantener la cabeza.
- Déficits en todas las áreas de la función motora.
- No puede sentarse o levantarse de forma autónoma ni con ayudas técnicas.
- No puede realizar movilidad independiente, aunque puede ser capaz de usar una silla de ruedas eléctrica.

Figura 3. GMFCS. Escala de clasificación de la motricidad gruesa para personas con parálisis cerebral (adaptada de www.canchild.ca/en/).

En relación a los objetivos terapéuticos de la parálisis cerebral, cabe destacar que el énfasis se coloca en conseguir aumentar la funcionalidad, mejorar las capacidades y mantener la salud en términos de locomoción, desarrollo cognitivo, interacción social e independencia. Sin duda, los mejores resultados resultan de una intervención temprana intensiva multidisciplinar con un enfoque holístico del tratamiento. El programa de tratamiento debe englobar la terapia física y la intervención comportamental, los tratamientos farmacológicos y quirúrgicos, el entrenamiento de la funcionalidad con ayudas técnicas y el tratamiento de los trastornos asociados, entre ellos, el dolor.

En este sentido, se ha puesto de manifiesto repetidamente que las condiciones secundarias a la parálisis cerebral pueden precipitar trastornos asociados, que en ocasiones, pueden ser de gravedad (Krigger, 2006). Por ejemplo, el déficit en la función motora oral, puede precipitar episodios de hipoxemia, contracturas temporo-mandibulares, vómitos y neumonías por aspiración asociadas con el, también frecuente, reflujo gastroesofágico. La reducida masa ósea en pacientes sin capacidad de locomoción, aumenta el riesgo de osteoporosis y fracturas. Asimismo, la salud mental puede verse afectada por el dolor crónico, el aislamiento social y la falta de funcionalidad e independencia.

El número de adultos con parálisis cerebral se ha visto incrementado por el aumento de la supervivencia de niños nacidos con factores de riesgo y por el incremento de la longevidad de la población adulta (O'Shea, 2008). Comparados con la población general, los adultos con parálisis cerebral presentan mayor mortalidad por enfermedades cardiacas isquémicas, enfermedades cerebrovasculares y problemas digestivos. La movilidad y habilidad para llevar a cabo actividades de la vida diaria disminuye con la edad, como ocurre en la población general, pero también disminuye el acceso a ayudas técnicas y a la adaptación de servicios, ya que las ayudas sociales y los accesos a los servicios sanitarios se ven reducidos en la población adulta con esta patología.

En el caso del dolor, numerosas investigaciones lo han identificado como una preocupación significativa y relacionada con el aumento de la edad, la disminución de la funcionalidad y la inactividad en personas adultas con parálisis cerebral (Murphy 2010; Tarsuslu & Livanelioglu, 2010, Turk, 2009). Según Vogtle (2009), aunque los problemas ortopédicos, la pobre densidad mineral ósea y las fracturas y los problemas mandibulares, dentales y de alimentación han sido sugeridos como fuentes de dolor en adultos con parálisis cerebral, la influencia de estas posibles causas no ha sido bien

estudiada. Aunque la literatura también apunta a que ciertos tratamientos como la toxina botulínica, el baclofeno intratecal, el ejercicio y el biofeedback podrían ser efectivos para minimizar el dolor, el pequeño tamaño de las muestras no permite establecer su efectividad. También se ha demostrado que aunque el dolor sólo interfiere moderadamente en la participación en actividades diarias de las personas adultas con parálisis cerebral, estos individuos no consultan a sus médicos cuando tienen dolor y utilizan menos los servicios de salud preventiva y rehabilitación. En este complejo contexto, y con el propósito de prevenir que futuras generaciones de personas con parálisis cerebral experimenten altos niveles de dolor, es necesario determinar sus causas y las intervenciones que pueden ser efectivas, fácilmente accesibles y asequibles.

Con el objeto de ofrecer un marco teórico apropiado para englobar el presente trabajo de investigación, los siguientes apartados de esta tesis doctoral ofrecen una breve descripción de la literatura científica sobre los déficits somatosensoriales que se presentan habitualmente en personas con parálisis cerebral (dolor y déficit en la sensibilidad somestésica), así como su relación con el trastorno motor presente en estos individuos.

1.2. Déficits somatosensoriales en personas con parálisis cerebral

La sensibilidad somestésica

Aunque clásicamente la parálisis cerebral se ha descrito principalmente como un trastorno motor, también se ha señalado que se trata de una patología que puede presentar trastornos asociados como epilepsia, problemas de crecimiento, déficits cognitivos y déficits en la percepción sensorial, como puede ser una percepción alterada de la sensibilidad dolorosa y táctil. En la actualidad, el tratamiento de las personas con parálisis cerebral se centra prioritariamente en el déficit motriz, desestimando la importancia de otros factores como la sensibilidad somestésica. Sin embargo, una información sensorial adecuada representa un componente esencial de la función motora y su control (Cooper et al., 1995; Nashner et al., 1983). Un ejemplo de ello son los resultados de experimentos con roedores, demostrando que los trastornos motores similares a los de las personas con parálisis cerebral eran reproducidos de forma más

fiable en ratas con restricción sensoriomotora de los miembros durante su desarrollo que por la asfixia perinatal (Strata et al., 2004). En este sentido, la existencia de deficits en la percepción somatosensorial implicaría la aplicación en la práctica clínica de la evaluación somestésica como parte integral de la valoración de las personas con parálisis cerebral y su tratamiento supondría maximizar el potencial de estas personas (Cooper et al., 1995).

Existen numerosas referencias en la literatura que demuestran que las personas con parálisis cerebral presentan disfunciones somatosensoriales relevantes. Hace más de dos décadas, Curry & Exner (1988) alertaron de que los niños con parálisis cerebral podían tener un alto riesgo de padecer trastornos somatosensoriales que podrían afectar a su función manual. Estas conclusiones se extrajeron de un estudio donde se comparó los objetos que preferían 15 lactantes sanos y 15 lactantes con parálisis cerebral. En ese estudio, se presentaron a los niños cinco objetos de distintas texturas para que los tocaran sin verlos. Los niños con parálisis cerebral eligieron objetos duros con más frecuencia que los niños sanos, mientras que estos últimos, no presentaron preferencia significativa por ningún objeto en particular. Los autores atribuyeron la aparente preferencia de los niños con parálisis cerebral por los objetos duros a una percepción táctil disminuida y a una necesidad de obtener estímulos propioceptivos mayores.

Posteriormente, diversos autores han utilizado pruebas sensitivas como la diferenciación de texturas, la discriminación entre dos puntos o la esterognosia para valorar los déficits en la sensibilidad táctil de las personas con distintos tipos de parálisis cerebral (Wingert et al., 2008; Sanger & Kukke, 2007; Yekutiel et al., 1994; Lesny et al.1993; Van Heest et al., 1993). La mayor parte de trabajos han evaluado las diferencias en la sensibilidad táctil de los miembros superiores entre personas sanas y personas con parálisis cerebral. De esta forma, se ha demostrado que entre el 51 y 97% de los niños y adultos jóvenes con parálisis cerebral presentan valores inferiores a los niños sanos en la discriminación táctil. Aunque se ha observado que la sensibilidad táctil es inferior con respecto a los controles sanos en todos los tipos de parálisis cerebral, Lesny et al. (1993) intentó determinar si esta pérdida sensitiva era mayor en unos tipos concretos de parálisis cerebral, descubriendo que estos déficits se presentaban de forma más frecuente en el tipo espástico y menos frecuente en el tipo atetoide.

También se ha examinado la sensibilidad profunda, mediante la valoración de la cinestesia y la propiocepción (Van Heest et al., 1993; Wingert et al., 2009). De esta

forma, Wingert et al. (2009) examinó la posición articular y cinestesia en el movimiento de rotación de antebrazos y caderas en dos muestras de individuos, sanos y con parálisis cerebral, con y sin visión del miembro examinado. Mientras que no se obtuvieron diferencias entre grupos en los ensayos con visión del miembro, hubo un aumento significativo de errores al determinar la posición articular y la sensación de movimiento pasivo en el grupo de parálisis cerebral, con sesgos que iban siempre hacia la posición de rotación interna, indicando una propiocepción pobre en la población con parálisis cerebral en todos sus miembros.

El test utilizado en la valoración parece que puede determinar el resultado de la prueba somatosensorial. En un estudio realizado en niños hemipléjicos (Van Heest et al., 1993), se encontró que el 97 % de los miembros espásticos presentaban deficits de estereognosia, el 90% presentaban déficits de discriminación entre dos puntos y el 46% de ellos presentaba déficits de propiocepción. Además, la afectación de la estereognosia correlacionaba con la disminución del perímetro del miembro, resultando de gran utilidad para establecer objetivos realistas al plantear la cirugía de este tipo de personas.

Se han realizado pocos estudios en zonas distintas a los miembros superiores. Entre ellos, y por su incorporación de la valoración conjunta de la sensibilidad y el dolor, podríamos destacar el estudio prospectivo longitudinal de cohortes de McLaughlin et al. (2005). En dicho estudio se examinó el dolor, el tacto fino, la dirección de rascado y la percepción de la vibración de los miembros inferiores y la posición de los dedos del pie y de la rodilla de 62 niños con parálisis cerebral y 65 niños sanos, obteniendo diferencias significativas entre ambos grupos en la percepción de la dirección del rascado, la percepción de la vibración y la percepción de la posición de los dedos del pie. Posteriormente, estos autores determinaron que la rizotomía dorsal no producía cambios en la función sensorial de los miembros inferiores de estos niños.

Un grupo reducido de estudios ha incorporado la medida de los potenciales evocados somestésicos (SEP) en los estudios de la sensibilidad en parálisis cerebral. Los SEP se han empleado en la investigación sobre la parálisis cerebral en dos tipos principales de estudios: los estudios que utilizan los SEP como prueba pronóstica del desarrollo de la patología en niños de riesgo, y los estudios que utilizan los SEP para comprobar la eficacia de tratamientos como la toxina botulínica. El primer grupo de estudios demostró que las anomalías los SEP neonatales, podría indicar una patología neurológica futura, como la parálisis cerebral (Suppiej et al., 2010; Ekert et al., 1997;

Pierrat et al., 1997; Gibson et al., 1992). En el segundo grupo de estudios, se puso de relevancia que una intervención en la condición espástica de un músculo, causada por la inyección de toxina botulínica, provocaba una normalización de los SEP y, por lo tanto, una modulación de las fibras aferentes que se atribuyó a la modulación del loop central del reflejo de estiramiento (Frascarelli et al., 2011; Boćkowski et al., 2007; Park et al., 2002). Esta influencia de una intervención periférica en los SEP también se demostró tras la utilización de unas ortesis de presión en niños con diplejia espástica (Kerem et al., 2001). En el estudio específico de los déficits sensitivos de la parálisis cerebral, Cooper et al. (1995) realizaron un estudio comparativo entre niños con parálisis cerebral y controles sanos utilizando test sensoriales y SEP. En este estudio, se observaron deficits bilaterales en la esterognosia y propiocepción en el 88.8% de los niños con parálisis cerebral. Además, la extensión de la pérdida sensorial no correlacionaba con la severidad de la afectación motora en los tests sensoriales, pero sí con los resultados de los potenciales evocados somestésicos.

Las causas de estos trastornos en la percepción de la sensibilidad somestésica han sido clasificadas clásicamente como primarias y secundarias. Las causas primarias obedecerían a lesiones en las áreas somatosensoriales corticales y subcorticales, mientras que las secundarias se deberían a los efectos que producen las alteraciones motoras, limitando las oportunidades de exploración sensorial y produciendo un feedback propioceptivo aberrante de los movimientos (Clayton et al., 2003). Recientes estudios de neuroimagen han probado alteraciones en las fibras de sustancia blanca que conectan con el córtex sensorial, lo que sugeriría que las lesiones de la parálisis cerebral provocan una ruptura de las vías de aferencia sensitiva, además de afectar a los tractos de eferencias motrices. En este sentido, Hoon et al. (2002) examinaron las vías de sustancia blanca de dos niños con parálisis cerebral del tipo tetraplejia espástica. El estudio demostró que las vías corticoespinales hasta el tallo cerebral eran similares a las de las personas sanas, pero las regiones posteriores del cuerpo calloso, cápsula interna y corona radiata estaban marcadamente reducidas, sobre todo en las fibras de sustancia blanca que conectaban con el córtex sensorial. Estos autores ampliaron su estudio a 28 niños pretérmino con parálisis cerebral y a 35 niños sanos, corroborando la existencia de lesiones más severas en las vías talámicas posteriores que en los tractos corticoespinales descendentes (Hoon et al., 2009). Además, observaron que las lesiones en los tractos talámicos posteriores correlacionaban con una sensibilidad táctil y propioceptiva

contralateral reducidas y con la severidad en la afectación motriz, mientras que las lesiones en las vías corticoespinales no correlacionaban con ninguna medición motora o sensorial. En el mismo sentido, Thomas et al. (2005) encontraron una reducción y degeneración primaria de la radiación talámica superior y degeneración secundaria en el cuerpo calloso, cabeza del caudado y núcleo lentiforme en cinco niños con parálisis cerebral hemiparésica. Más recientemente, Coq et al. (2008) realizaron un estudio con ratas adultas sometidas a asfixia perinatal y a desuso de los miembros durante su desarrollo madurativo. Las ratas con restricción sensoriomotora, con o sin asfixia prenatal, presentaron una desorganización topográfica en la representación del miembro en la corteza S1, con aumento de las respuestas corticales y disminución de la selectividad neuronal para las aferencias sensoriales. Estos resultados sugirieron que los patrones monótonos y estereotipados de los niños con parálisis cerebral podían procurar un feedback sensorial anormal, alterar la reorganización cortical y producir déficits en el procesamiento sensorial en esta población.

Algunos autores han sugerido además que una anormal percepción somatosensorial mantenida desde edades tempranas podría, de forma potencial, causar cambios a largo plazo en el procesamiento de la información sensitiva y dolorosa, de forma que una sensibilidad táctil pobre puede relacionarse con una mayor sensibilidad al dolor en niños con lesiones cerebrales tempranas, como puede ser la parálisis cerebral (Schmelzle-Lubiecki et al., 2007).

La percepción del dolor en la parálisis cerebral

Como hemos expuesto anteriormente, las personas con parálisis cerebral padecen deficiencias del control y la coordinación motora, déficits funcionales, problemas sensoriales y en ocasiones, déficits cognitivos y dificultades de comunicación. En este complejo contexto, una revisión de la literatura realizada por McKerarnan et al. (2004) puso de manifiesto que, aunque el dolor es una experiencia común en personas con parálisis cerebral, los mecanismos neurobiológicos y psicosociales subyacentes han sido muy poco investigados. Estos autores afirman que el dolor puede deberse tanto a problemas de la patología en sí misma, como a procedimientos médicos, quirúrgicos o rehabilitadores que la patología suele requerir de forma regular.

Uno de los trabajos pioneros en este campo fue el de Turk et al. (1997), que realizaron una encuesta de salud en 63 mujeres adultas (entre 20 y 74 años) con parálisis cerebral y residentes en la comunidad. El nivel de salud se midió mediante 4 criterios: su percepción de salud, condiciones asociadas (retraso mental o dificultades de aprendizaje), condiciones secundarias (dolor, problemas ortopédicos y viscerales o salud dental) y comportamientos saludables (consumo de alcohol y tabaco, dieta, actividad física, revisiones médicas,…). Los resultados del estudio mostraron que, en general, las mujeres se consideraban saludables, no tenían hábitos tóxicos, seguían una dieta equilibrada y practicaban ejercicio físico. Sin embargo, se encontraron altos porcentajes de problemas secundarios, como deformidades en caderas y espalda, problemas intestinales y vesicales, reflujo gastroesofágico y una pobre salud dental. En este estudio, el dolor aparece como una condición secundaria frecuente en las personas con parálisis cerebral (aparecían problemas de dolor en el 84% de la muestra) y se encontraron asociaciones, aunque sin significación estadística, entre éste y el grado de retraso mental. Además, el 56% de las mujeres estudiadas, refirieron una limitación de sus actividades a causa del dolor.

Un segundo estudio realizado por Schwartz et al. (1999) donde se entrevistaba a 93 adultos con parálisis cerebral, confirmó que el porcentaje de sujetos con dolor crónico se situaba en torno a 67% y que la mayoría señalaba dolor en diversas regiones desde hacía varios años. Los dolores más frecuentes se localizaron en los miembros inferiores (66% de la muestra) y espalda (63%). La intensidad dolorosa, medida en una escala EVA de 11 puntos, fue mayor de 5 en el 53% de los sujetos y se observó un progresivo aumento asociado a la edad.

Posteriores estudios han reiterado que el dolor en las personas con parálisis cerebral es mayor que el padecido por las personas sanas. Los niveles de prevalencia del dolor en los adultos con parálisis cerebral han variado entre el 25% y el 75% (Gallien et al., 2007; Odding et al., 2006; Jahnser et al., 2004; Engel et al., 2003) y en niños entre el 48% y el 79% (Parkes et al., 2009; Russo et al., 2008; Tervo et al., 2006; Engel et al., 2005; Breau et al., 2003). El dolor se presentaba de forma constante o diaria en la mitad de los individuos afectados y con una intensidad dolorosa de 2 a 4 en una escala de 0-10 (Engel et al., 2003, 2005; Breau, 2003). Una de las causas principales de dolor, tanto en la población infantil como en la población adulta, eran los problemas musculoesqueléticos (Jahnser et al. 2004; Breau et al., 2003) que se manifestaban en

múltiples localizaciones, predominando en la zona lumbar, caderas, miembros inferiores y miembros superiores (Jóźwiak et al., 2010; Doralp & Bartlett, 2010; Gallien et al., 2007; Castle et al., 2007; Krigger, 2006; Jahnsen et al., 2004; Engel et al., 2003; Dudgeon et al., 2002). Además del dolor ocasionado por las alteraciones orgánicas propias de la patología, las intervenciones sanitarias a las que las personas con parálisis cerebral son sometidas desde su más tierna infancia, también se han revelado como consistentes fuentes de dolor (McKearnan et al., 2004; Hadden &Von Baeyer, 2002; Kibele, 1989). Además, las personas con parálisis cerebral pueden requerir intervenciones quirúrgicas con más frecuencia que las personas sanas y deben soportar las molestias causadas por el manejo, inmovilidad y ayudas técnicas que no siempre ajustan de forma adecuada (Lannin et al., 2008).

Las repercusiones de este dolor alcanzan múltiples niveles en la vida de las personas con parálisis cerebral. Por una parte, en la población adulta, el dolor puede interferir con la capacidad de locomoción, el equilibrio, la fatiga física (Opheim et al., 2007; Jahnsen et al., 2004) y, en general, con su independencia y su capacidad de participar en actividades de la vida diaria (Castle et al., 2007; Tervo et al., 2006; Engel et al., 2003). En la población infantil, se ha mostrado que el dolor interfiere con el movimiento, los programas de educación física, la actividad escolar, el sueño y el autocuidado, haciendo a los niños más dependientes (Russo et al., 2008; Berrin et al., 2007; Tervo et al., 2006). Recientemente, Malone y Vogtle (2009) demostraron que el número de zonas dolorosas correlacionaba con la capacidad para realizar actividades diarias. En el estudio de Engel et al. (2003), las personas que tenían dolor indicaron elevados niveles de estrés psicológico y moderada satisfacción con la vida, aunque la interferencia del dolor con sus actividades diarias fuese catalogado como menor (puntuaciones de 2 a 3 en una escala de 0-10).

Parece existir un consenso en la literatura que indica que el dolor disminuye la calidad de vida en personas con parálisis cerebral, independientemente de su edad. Los adultos con parálisis cerebral que padecen dolor suelen manifestar elevados niveles de soledad, frustración y estrés psicológico y una moderada satisfacción con la vida (Castle et al., 2007; Jahnser et al., 2004; Engel et al. 2003). Con respecto a la calidad de vida de los niños con parálisis cerebral, un estudio europeo llevado a cabo mediante cuestionarios realizados a niños con parálisis cerebral entre 8 y 12 años demostró que estos niños tenían la misma calidad de vida que los niños sanos, aunque el dolor hacía que esta

calidad de vida disminuyera en todos los aspectos (Dickinson et al., 2007). Este mismo estudio realizado con los padres asoció también la presencia de dolor a una pobre calidad de vida en los dominios de bienestar físico y psicológico y en la percepción de uno mismo (Arnaud et al., 2008). Todos estos resultados coinciden con los presentados por Bjornson et al. (2008), donde los niños con parálisis cerebral percibieron igual calidad de vida que sus compañeros sanos aunque percibieran un estado de salud menor en las subescalas concernientes al comportamiento social, función física, salud general y dolor.

Casi un tercio de los sujetos adultos con parálisis cerebral se manifestaron insatisfechos con la atención y tratamiento que recibía su problema de dolor (Engel et al., 2003). Krigger et al. (2006) llegaron a afirmar que sólo el 14% de los adolescentes y adultos con parálisis cerebral y sin capacidad de movimiento que experimentan dolor, reciben tratamiento adecuado, a pesar de que las causas iatrogénicas de dolor, como las movilizaciones, las palpaciones y el soporte de peso con las extremidades inferiores eran las más habituales. Estos resultados concuerdan con los aportados por Dudgeon et al (2002), quienes encontraron que el dolor no era monitorizado sistemáticamente por los trabajadores sanitarios. No obstante, otros informes ponen de relieve que existen divergencias en las percepciones que realizan los propios individuos y el personal sanitario. Así, por ejemplo, Hilberink et al. (2007) compararon autoinformes de adultos jóvenes con parálisis cerebral y cuestionarios de sus médicos rehabilitadores y observaron que las personas con parálisis cerebral relataban menor frecuencia de dolor que las apuntadas por sus médicos (59% frente al 88%). Estos cuestionarios también mostraron una reducida utilización de los servicios de salud por parte de personas adultas con parálisis cerebral.

El dolor se ha asociado a diferentes variables como la edad, género, déficit motor, fatiga crónica, baja satisfacción con la vida, síndrome depresivo, trastornos del sueño y deterioro de la función física de personas con parálisis cerebral (Jahnsen et al., 2004; Castle et al., 2007). Breau et al. (2003) encontraron que la edad también era un factor predictor de la existencia de dolor en las personas con parálisis cerebral. A este respecto, los autores descubrieron que una edad inferior a 7 años, unida a otros factores, podía predecir ciertos tipos de dolor. Estos resultados contrastan con otro estudio realizado con población adulta, en el que se demostró que el dolor aumentaba con la edad (Schwartz et al., 1999).

Otro factor que ha sido especialmente estudiado en pacientes con parálisis cerebral es la relación entre percepción dolorosa y afectación motora. No obstante, los resultados obtenidos hasta la fecha son poco esclarecedores y contradictorios. Por ejemplo, Houlihan et al. (2004) encontraron una estrecha asociación entre el dolor padecido por niños con parálisis cerebral y la severidad de su déficit motor (los niños con mayor afectación motora, presentaban dolores más frecuentes, mayor pérdida de días de escuela y mayor número de días en cama). Por el contrario, Kennes et al. (2002) observaron que el dolor no se asociaba al grado de limitación funcional descrito con el GMFCS, aunque sí que se encontraron correlaciones significativas entre los valores del GMFCS y la movilidad, la destreza, la expresión oral, la visión, la audición y la cognición.

En conclusión, parece que las personas con parálisis cerebral padecen dolor frecuente, de localización múltiple y de intensidad entre moderada y severa a cualquier edad. Este dolor interfiere con sus actividades diarias y provoca una disminución de su calidad de vida, asociándose a sentimientos de frustración, soledad y depresión. Este dolor no parece ser suficientemente monitorizado ni tratado por el personal sanitario. Estos datos sugieren que el dolor es un problema de gran importancia en personas con parálisis cerebral y que es probable que la investigación dedicada a profundizar en sus mecanismos de producción, mantenimiento o alivio pueda aportar información útil para mejorar la calidad de vida de estas personas. Por otro lado, dada la estrecha relación existente entre sensibilidad táctil y dolor, así como la posibilidad de que las experiencias dolorosas tempranas y mantenidas en el tiempo puedan llegar a modificar a largo plazo el procesamiento de las aferencias sensoriales y nociceptivas (Schmelzle-Lubiecki et al., 2007), la investigación de la percepción somatosensorial en pacientes con parálisis cerebral representa un tema científico de interés clínico. El conocimiento de los procesos fisiológicos que afectan a la percepción somestésica puede proporcionar las claves para implementar tratamientos destinados evitar la sensibilización dolorosa y, por lo tanto, la perpetuación del dolor en las personas con parálisis cerebral.

Relación entre los déficits somatosensoriales y motores en la parálisis cerebral

La disfunción motora en las personas con parálisis cerebral se ha atribuido tradicionalmente al daño estructural del tracto corticoespinal. No obstante, Hoon et al. (2002) afirmaron que el daño de las fibras de sustancia blanca afectaba a las fibras aferentes somatosensoriales en mayor medida que a los tractos motores descendentes. Estos autores encontraron una correlación entre el daño de la radiación talamocortical posterior y diversas medidas de afectación motora. Este descubrimiento ponía en entredicho la asunción tradicional de que la afectación motriz en la parálisis cerebral era provocada sólo por la lesión de las vías descendentes. A raíz de la reconocida importancia de las aferencias somatosensoriales en la función motora y, especialmente, debido al hecho de que la patología afecta a un sistema nervioso en desarrollo (Clarac et al., 2004), es lógico pensar que una lesión que afecte a estas aferencias sensoriales podría estar detrás del trastorno motor clínicamente predominante (Wilke & Staudt, 2009).

La influencia de las aferencias somatosensoriales en la correcta consecución de la acción motora ha sido abordada frecuentemente por diversos estudios neurofisiológicos y clínicos. Está ampliamente admitido que el cuerpo estriado, estructura crítica en la ejecución y el aprendizaje de tareas motoras, recibe aferencias somatosensoriales. Pidoux et al. (2010) en un estudio reciente con roedores describieron que el flujo somatosensorial que llegaba al cuerpo estriado permitiría la selección de distintas neuronas medioespinales funcionalmente significativas durante un determinado acto motor. También se admite desde hace años que el 40% de las fibras del tracto corticoespinal proceden del Área 5 de S1, cuyos axones proyectan predominantemente en el asta posterior conectando con motoneuronas gamma (Rathelot & Strick, 2006; Seki et al., 2003; Galea & Darian-Smith, 1994). En estudios con primates se demostró una coherencia corticomuscular en la banda de frecuencia beta entre S1 y la musculatura periférica, con una mayor fuerza de la señal en la dirección S1-músculo (Witham et al., 2010). Curiosamente, la latencia de la señal de S1 al músculo fue menor que la de M1 al músculo. Además se comprobó la existencia de coherencia en la banda de frecuencia beta entre M1 y S1. Los autores exploraron cuatro hipotéticas vías de comunicación entre M1, S1 y el músculo. Estas vías están ilustradas en la Figura 4 y

hacen referencia a: 1) señales de M1 y S1 hacia el músculo, que están sincronizadas por las aferencias recibidas de otra región cerebral, como el área motora suplementaria o SII; 2) oscilaciones de S1, que se propagarían a M1 y después a la periferia; 3) aferencias enviadas desde el área 3a hacia las motoneuronas gamma, que mediante la regulación de los husos neuromusculares influirían en las motoneuronas alfa; 4) aferencias desde M1, que irían simultáneamente hacia la corteza somatosensorial y el músculo. Los autores concluyeron que la corteza somatosensorial recibe una copia de la orden motora que sale desde M1 hasta el músculo, de forma que S1 podría predecir no sólo el movimiento final sino también sus consecuencias sensoriales.
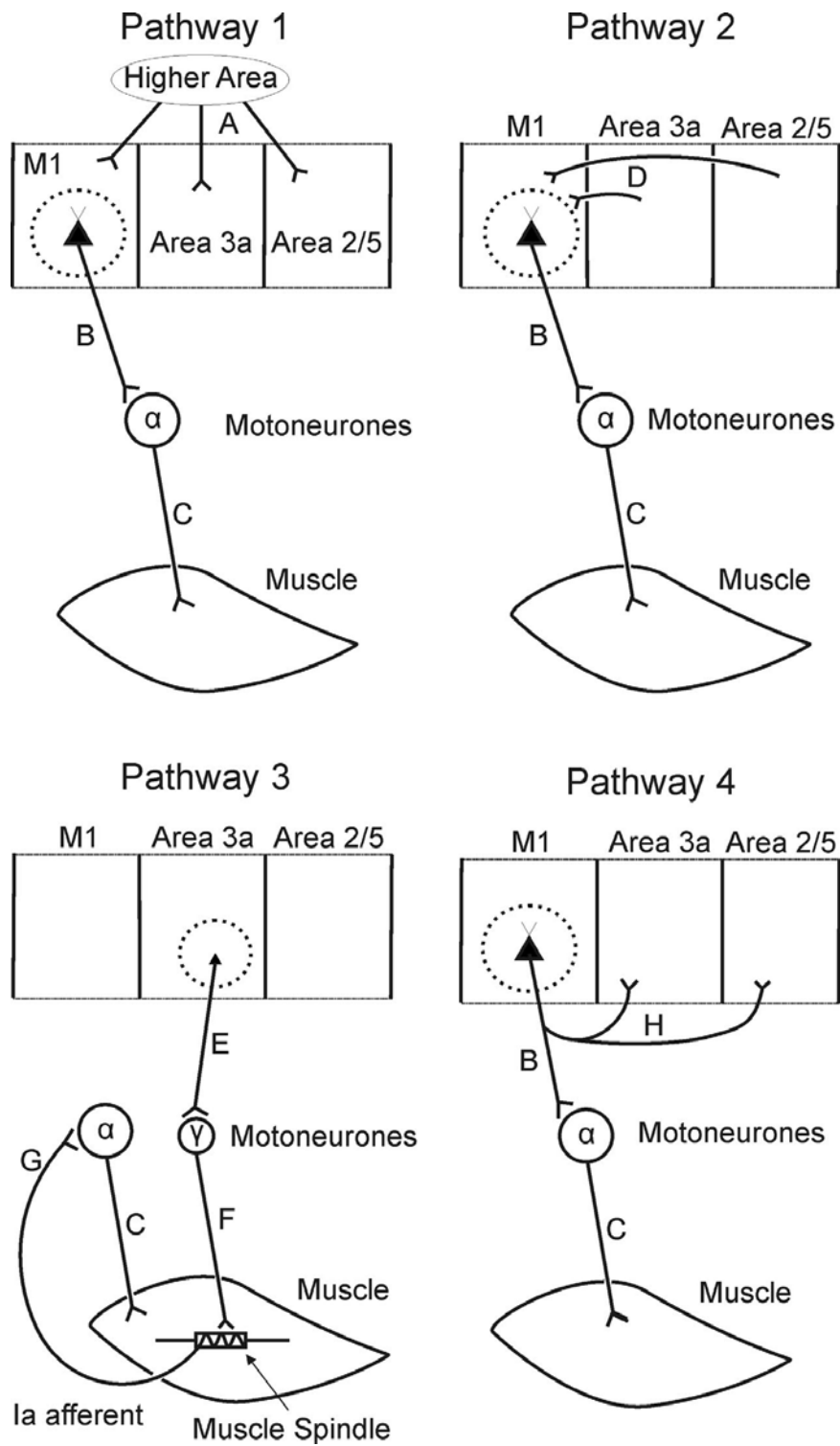
Figura 4. Representación esquemática que muestra las posibles vías implicadas en la coherencia entre S1/area 5 y EMG. (extraído de Witham CL, Wang M, Baker SN. Corticomuscular coherence between motor cortex, somatosensory areas and forearm muscles in the monkey. Front Syst Neurosci. 2010; 30;4. pii: 38).

Estudios con roedores han demostrado que existe una estrecha relación entre las aferencias sensoriales, las vías descendentes y las motoneuronas. Este sistema comenzaría a desarrollarse en las etapas prenatales y jugaría un papel clave en la maduración de la locomoción y su control neural (Clarac et al., 2004). Dado que la parálisis cerebral está causada por lesiones cerebrales acaecidas durante el desarrollo del SNC, parece bastante probable que los mecanismos que permiten el desarrollo de movimientos esenciales, como la locomoción, se encuentren afectados.

Numerosos estudios con humanos también sugieren una asociación de las áreas parietal, premotora y motora durante la preparación y ejecución de los movimientos (Ziluk et al., 2010; Iseki et al., 2010; La Pointed et al., 2009; Wheaton et al., 2005). Por ejemplo, se ha comprobado que S1 interviene en la regulación de la fuerza de los movimientos prensiles de precisión (Haller et al., 2010) o que el procesamiento propioceptivo y vestibular contribuye a construir modelos internos que asientan y actualizan el sentido de la verticalidad y la postura bípeda (Barra et al., 2010). Se ha sugerido incluso, que el aprendizaje motor también produce cambios en las áreas somatosensoriales cerebrales, que a su vez, mejorarían la acción motora (Ostry et al., 2010). Así, un estímulo somatosensorial continuado puede aumentar la representación cortical de los músculos sobre los que se aplica (Meesen et al., 2010). Por otra parte, se ha comprobado que la pérdida de sensibilidad, reduce la eficacia de la tarea motora y alarga el tiempo de reacción (Boudreau et al., 2010, Vidoni et al., 2010).

La presencia de dolor también es capaz de condicionar el acto motor. De hecho, numerosas conexiones cerebrales asocian estructuras consideradas clásicamente motrices con estructuras de la red nociceptiva. El cortex motor está implicado en la modulación del dolor (Xie et al., 2009). La ínsula posterior, que juega un importante papel en el procesamiento de estímulos nociceptivos, presenta conexiones no sólo con S1, sino también con M1 (Peltz et al., 2011). Además se ha comprobado que el cerebelo, estructura asociada clásicamente al acto motor, recibe y regula aferencias nociceptivas tanto en casos de dolor agudo como de dolor crónico (Moulton et al., 2010) y que los ganglios basales participan en el eje tálamo-córtico-basal, regulando la integración de las respuestas motoras, emocionales, cognitivas y autónomas ante el dolor (Boorsook et al., 2010). Además, las aferencias nociceptivas llegan a modular la neuroplasticidad en M1 asociada con el entrenamiento motor y pueden alterar la capacidad de aprendizaje de nuevas tareas motrices (Boudreau et al., 2007).

Experimentos clínicos han confirmado que el dolor aumentaba la presencia de errores y enlentecía el tiempo de reacción en una tarea motora (Boudreau et al., 2010; Babiloni et al., 2010). Además, se ha observado que la presencia de dolor experimental en individuos sanos producía cambios en el EMG que reflejaban una mayor activación muscular y un acortamiento del tiempo de descanso (Samani et al., 2009).

La integridad de las aferencias somatosensoriales y del sistema musculoesquelético son componentes esenciales del control y desarrollo de la función motora. Se ha demostrado que déficits en las aferencias periféricas o en su procesamiento a nivel central pueden interferir con la planificación y la ejecución del acto motor (Lourenço et al., 2007; Schmelzle-Lubiecki et al., 2007, Abbruzzese & Berardelli, 2003). También se ha comentado que el grado de preservación del procesamiento sensorial central influye en la capacidad de aprendizaje motor tras una lesión. Por ejemplo, este aprendizaje se mostró directamente relacionado con la integridad del procesamiento propioceptivo en personas que habían sufrido un ictus (Vidoni & Boyd, 2009).

Si nos centramos en las personas con parálisis cerebral, varios autores han establecido una relación entre el déficit de integración sensoriomotora y la falta de control anticipatorio en movimientos de prensión (Van Elk et al., 2010; Gordon et al., 2006; Duff & Gordon, 2003) o de mantenimiento del equilibrio en bipedestación (Cherng et al., 1999). Eliasson et al. (1991) afirmaron que los retrasos entre las sucesivas fases de un acto motor que presentan las personas con parálisis cerebral indicaban un feedback sensorial ineficaz durante el movimiento. Además, estudios con personas con parálisis cerebral hemiparética, cuya reorganización cortical recolocó M1 en el hemisferio ipsilateral al lado parético y a S1 en el hemisferio contralateral, demostraron una menor asociación no sólo entre M1 y S1, sino también entre M1 y el músculo, así como menor coherencia corticomuscular con S1 durante el acto motor (Gerloff et al., 2006). Por otra parte, se ha sugerido que el sistema motor y premotor pueden influir en la organización de la corteza somatosensorial (Kirimoto et al., 2010; Ito et al., 1981). Esto puede ser de especial importancia en una patología como la parálisis cerebral, ya que los patrones de movimientos estereotipados y los problemas motrices que reducen la capacidad exploratoria del niño pueden conducir a un feedback sensorial anormal y a una reorganización cortical alterada, perpetuando así los déficits somatosensoriales (Coq et al., 2008, Clayton et al.; 2003).

La comprensión de los mecanismos de plasticidad del SNC tras la lesión temprana ocurrida en esta patología, ayudará a desarrollar programas de tratamiento que mejoren la funcionalidad. La extensión de los cambios neuroplásticos puede ser clave en el grado de recuperación funcional, por lo tanto, las intervenciones que intenten maximizar la adecuada reorganización cortical, serán las que tengan mayor potencial rehabilitador. Teniendo en cuenta que la plasticidad cerebral puede ser dependiente del aprendizaje, las intervenciones que puedan actuar sobre la organización del sistema somatosensorial, podrían influir en la evolución de los signos motores en las personas con parálisis cerebral (Eyre, 2007; Flor, 2003). El estudio de los mecanismos de reorganización de estructuras cerebrales dañadas podría llevar a nuevas aproximaciones en la rehabilitación de estas personas.

1.3.   La hipótesis de un déficit sensoriomotor en la parálisis cerebral

A pesar de que la definición de parálisis cerebral señala que los problemas motores de esta patología se acompañan frecuentemente de trastornos de la sensibilidad, estas anormalidades sensitivas habían sido clásicamente estimadas simplemente como una pequeña parte del complicado conjunto de afectaciones que influían en la evolución y pronóstico de la lesión motora de las personas con parálisis cerebral. Sin embargo, existen estudios neurofisiológicos que intentan utilizar las anomalías presentes en los potenciales evocados somatosensoriales (SEP) de los niños con riesgo perinatal, como factor pronóstico de parálisis cerebral (Görke, 1986). Por otra parte, algunos investigadores que centraban sus estudios en la función manual y la manipulación de objetos de las personas con parálisis cerebral, comenzaron a considerar influencia de las variables sensitivas en la ejecución de la acción motriz manual (Eliasson et al., 1991; Steenbergen et al., 1998; Duff & Gordon, 2003). No obstante, el detonante que hizo plantear la hipótesis de que el daño en los circuitos somatosensoriales sustentaba el déficit motor en la parálisis cerebral fueron los trabajos publicados por Hoon et al. (2002, 2009), basados en el estudio de la afectación de las vías talamocorticales en la leucomalacia periventricular y su relación con el déficit motor. La demostración de que las vías talamocorticales se encontraban más dañadas que las vías corticoespinales, permitió a estos autores postular la hipótesis de que la lesión que determinaría las

características clínicas de la parálisis cerebral, sería la lesión de las vías sensitivas ascendentes en lugar de la lesión del tracto motor descendente (Hoon et al., 2002). Posteriormente, estos autores reforzaron su hipótesis al encontrar una correlación significativa entre las medidas de afectación motora y el daño de la vía talamocortical posterior (Hoon et al., 2009).

A raiz de estos descubrimientos, la comunidad científica, dentro de los distintos foros dedicados a la medicina del desarrollo, discapacidad pediátrica y parálisis cerebral, comenzó a replantearse la importancia de los déficits sensitivos en esta patología. La discusión llevada a cabo en estos foros, queda perfectamente plasmada en comentario publicado por Wilke & Stoud (2009) en la revista *Developmental Medicine & Child Neurology*, revista de referencia tanto de la *American Academy for Cerebral Palsy and Developmental Medicine* (AACPDM) como de la *European Academy of Chilhood Disability* (EACD). Por una parte, la contribución de las aferencias somatosensoriales a la ejecución motora era ya un hecho ampliamente aceptado, por lo que la hipótesis de que la anormalidad de estas aferencias subyaciese a la afectación motora, parecía plausible. Los trabajos sobre redes neuronales, que han demostrado la importancia de la contribución de las aferencias somatosensoriales a la ejecución motora, especialmente en un sistema nervioso en desarrollo (Clarac et al., 2004), se sitúan en este sentido, avalando la validez de esta hipótesis. Sin embargo, la hipótesis del déficit somatosensorial se sustenta en pocos estudios muy específicos, realizados solo sobre unas vías concretas que podrían estar desplazadas espacialmente en personas con patología y en muestras heterogéneas de pacientes. Esto ha hecho que las aportaciones de esta hipótesis se hayan considerado de un modo moderado por los foros científicos internacionales, que admiten la implicación de los déficits somatosensoriales de forma acompañante a la lesión de los tractos motores descendentes y su posible influencia en determinadas variables clínicas, como por ejemplo en el grado de las manifestaciones clínicas de los distintos subgrupos de parálisis cerebral. En este momento, la importancia real de esta hipótesis ha sido dar relevancia al sistema somatosensorial en el estudio de los mecanismos fisiopatológicos de la parálisis cerebral, sistema hasta ahora poco considerado por la comunidad científica en el estudio de esta patología, y propiciar el incremento de la investigación en esta área.

II

Objetivos de la presente investigación

En esta investigación nos proponemos examinar la existencia de déficits sensoriomotores en personas con parálisis cerebral, un trastorno caracterizado fundamentalmente por alteraciones motoras. El eje principal de este trabajo se centró en la exploración de distintas formas del sistema somatosensorial. Para ello, la presente investigación analiza principalmente dos fenómenos psicofisiológicos que se manifestaron esenciales en las personas con parálisis cerebral: 1) el dolor, debido a la alta incidencia y a las limitaciones funcionales que provoca en estas personas, y 2) la sensibilidad táctil, fuente esencial de aferencias para acciones motoras, sobre todo de los miembros superiores. Por una parte, tendríamos que corroborar la presencia de déficits en el sistema somatosensorial de las personas con parálisis cerebral que se describían en la literatura. Además, nos interesaba conocer las características del procesamiento somatosensorial, así como las características del procesamiento motor en personas con parálisis cerebral que presentaban déficits somatosensoriales. Por último, pretendíamos que nuestra investigación contuviese una vertiente clínica, en la que pudiese comprobarse si los conocimientos adquiridos en los estudios anteriores, podían aplicarse de forma eficaz al tratamiento de los problemas que presentan las personas con parálisis cerebral.

El objetivo general de esta investigación es comprobar como los posibles déficits en el procesamiento somatosensorial se relacionan con los déficits motores que presentan las personas con parálisis cerebral. Para ello, se han trazado los siguientes objetivos específicos:

1. Obtención de datos sociodemográficos acerca de la incidencia de problemas de sensibilidad táctil y dolorosa en la población con parálisis cerebral.

2. Profundización experimental en el procesamiento somatosensorial del dolor y la sensibilidad táctil.

3. Estudio experimental del procesamiento motor en personas con parálisis cerebral con trastornos somatosensoriales.

4. Evaluar la posible modificación de la sensibilidad somestésica, dolor y función motora mediante un programa de intervención terapéutica que se dirija a mejorar los déficits somatosensoriales encontrados en los pacientes con parálisis cerebral.

III

Parte experimental

Introducción general a los experimentos realizados

Como hemos expuesto en los apartados anteriores, las personas con parálisis cerebral presentan alteraciones en la sensibilidad somestésica y nociceptiva desde la primera infancia. La repercusión que una lesión producida a edades tempranas puede tener en el desarrollo del sistema nervioso y de sus funciones asociadas, en concreto, de la función somatosensorial, es un fenómeno complejo que implica, además de déficits en el funcionamiento asociados a la lesión de un sistema nervioso inmaduro, la posibilidad de reorganización del procesamiento de la información aferente a lo largo del tiempo. Además, es ampliamente admitido por la comunidad científica, que un adecuado procesamiento de la información sensorial es fundamental para la planificación y ejecución correcta de la acción motora. La presente investigación pretende profundizar en la hipótesis de que la parálisis cerebral, aunque considerada clásicamente como un trastorno motor, es una patología que presenta graves problemas en el procesamiento somatosensorial.

Centrándose en el objetivo de explorar la hipótesis de la existencia de déficits sensoriomotores en pacientes con parálisis cerebral, la presente investigación se desarrolló en diversas fases alrededor de los cuatro objetivos específicos que se mencionaron anteriormente. En particular, los cuatro objetivos se concretaron de la siguiente forma:

1. Examinar si la sensibilidad táctil y dolorosa de las personas con parálisis cerebral es diferente a la de voluntarios sanos en tres rangos de edad: infancia (entre los 6 y los 10 años), adolescencia (10-17 años) y adultos jóvenes (18-30 años).

2. Analizar si existen diferencias en el procesamiento cerebral asociados a la estimulación no dolorosa en personas con parálisis cerebral y voluntarios sanos mediante el registro de potenciales evocados somatosensoriales.

3. Comparar diferentes parámetros de la actividad motora y sus correlatos cerebrales en personas con parálisis cerebral y voluntarios sanos.

4. Evaluar la eficacia de un programa de terapia somatosensorial sobre los problemas táctiles, dolorosos, propioceptivos y motores en personas con parálisis cerebral.

A continuación, se realiza una breve presentación de los diferentes experimentos que componen la presente tesis doctoral, así como de las publicaciones científicas que hemos elaborado a partir de los resultados obtenidos y un apartado final dedicado a discutir globalmente los resultados y las conclusiones alcanzadas en la investigación.

Experimento 1. Sociodemografía de los déficits somatosensoriales en las personas con parálisis cerebral

Presentación de la investigación

La primera parte de nuestra investigación se centró en corroborar los datos descritos por la literatura acerca de la presencia de deficiencias en la percepción somatosensorial de las personas con parálisis cerebral. Para ello, nos centramos principalmente en la exploración de las características sociodemográficas de los dos parámetros que se habían considerado principales objetos de la exploración somatosensorial en la investigación: el dolor, debido a la alta incidencia y a las limitaciones funcionales que provoca en las personas con parálisis cerebral, y la sensibilidad táctil, fuente esencial de aferencias para acciones motoras, sobre todo de los miembros superiores.

El objetivo principal de esta fase de la investigación era comprobar si existían diferencias, en cuanto a variables fisiológicas, psicológicas y cognitivas, influyentes en el dolor y en la sensibilidad tactil, entre personas con parálisis cerebral y personas de la población general de distintas franjas de edad. Además, y dado que la literatura señalaba que los procedimientos sanitarios a los que estas personas son sometidas desde edades tempranas podrían tener una importante influencia a largo plazo sobre la exacerbación del dolor, y dada la trayectoria académica y profesional de la doctoranda (fisioterapeuta), se estudió cual era la repercusión de la actuación de estos profesionales en la percepción dolorosa de sus pacientes con parálisis cerebral.

Los resultados de esta fase del estudio se han plasmado en dos manuscritos que se adjuntan a continuación: *Age-related changes of pain experience in cerebral palsy and healthy individuals*, publicado en la revista Pain Medicine en 2011, y *Physical therapist actuation on the experience of pain in cerebral palsy.*

ORIGINAL RESEARCH ARTICLES

Age-Related Changes of Pain Experience in Cerebral Palsy and Healthy Individuals

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Abstract

Objective. Pain is a serious problem for many individuals with cerebral palsy (CP). Pain and injury in early life may cause long-term changes in somatosensory and pain processing. Nevertheless, no information exists regarding the influence of age on pain reports and touch sensitivity among persons with CP or the influence of age on the quality of life in individuals with CP.

Design. The present cross-sectional study investigated pain characteristics, touch sensitivity, and quality of life in 86 individuals with CP and 115 healthy volunteers. Participants were grouped by age in children (6–10 years), adolescents (11–17 years), and young adults (18–30 years). Touch sensitivity at different body locations were tested by using von Frey monofilaments. Data about pain and quality of life were obtained from a semi-structured interview and questionnaires.

Results. Participants with CP reported more pain as well as more reduced touch sensitivity and quality of life than healthy controls. Neither pain reports nor touch sensitivity or quality of life were influenced by age in CP, whereas significant age-related changes were observed in healthy participants. Multiple regression analyses also showed that age was the best predictor of current pain intensity in healthy controls but not in individuals with CP.

Conclusion. These findings emphasize the importance of considering the presence of pain at very early ages in CP. Furthermore, these results provide clinicians and researchers with a new age-related psychosocial and psychophysiological perspective to investigate the mechanisms that could be involved in the presence and maintenance of pain in this population.

Key Words. Cerebral Palsy; Quality of Life; Child Disability; Adolescence

Introduction

Recently, there has been a growing recognition that pain represents a serious problem for many children and adolescents with cerebral palsy (CP). Indeed, pain is perceived as a secondary problem in 47–78% of children and adolescents with CP [1–4]. Pain in CP is frequently described as moderate and is located mostly in the abdomen and in the musculoskeletal system [2,3]. Pain also seems to limit daily activities and satisfaction with life in children and adolescents with CP [1,4]. Moreover, it has been suggested that pain is one of the most significant factors influencing the quality of life in children with CP [5]. However, although children with CP have significantly lower health status concerning physical function and bodily pain than age- and sex-matched typically developing children, they have similar quality of life [6]. To date, research on pain in CP has been oriented primarily to the analysis of its influence on the quality of life without considering age-matched healthy controls. Such a comparison group would allow for the control of environmental factors that could influence pain and quality of life.

Pain and injury in early life may cause long-term changes in somatosensory and pain processing [7]. Therefore, it seems plausible that the developing nervous system of children and adolescents with brain damage may respond differently to pain and somatosensory information in early and later life. In this sense, several studies have shown that children with CP had poorer touch sensitivity, stereognosis, and proprioception compared with healthy children [8–10]. However, despite age-related differences in many chronic pain conditions, virtually nothing is known about pain and touch sensitivity in children and adolescents with CP.

The present study included three age groups (children, adolescents, and adults) of individuals with CP and healthy controls to examine pain, touch sensitivity, and quality of life. Based on previous work indicating that pain may play a key role in children with CP [1–6], we

hypothesized that younger participants with CP would show differences in pain and somatosensory perception and that differences between individuals with CP and healthy controls would appear in both younger and older subjects. Moreover, consistent with previous results showing that pain represents the most significant factor influencing quality of life in CP [5], we also explored age-related changes on quality of life and other factors affecting pain intensity in individuals with CP and healthy controls.

Methods

Participants

One hundred fifty persons with CP (50 children aged 6–10 years, 50 adolescents aged 11–17 years, and 50 young adults aged 18–30 years) and 150 healthy persons were initially contacted through a letter explaining the details of the study. Participants with CP were identified by physiotherapists from specialized centers for CP, whereas non-CP participants were recruited by asking for volunteers in educational centers, from primary schools to universities. Inclusion criteria were an age of 6–30 years and a cognitive level that allowed for the understanding of simple yes/no questions.

Eighty six subjects with CP (27 children, 24 adolescents, and 35 young adults) and 115 healthy subjects (34 children, 35 adolescents, and 46 young adults) agreed to participate in the study. For participants under the age of 18, permission and written informed consent from the center and from their parents or legal tutors were obtained. Healthy adults provided written informed consent and verbalized willingness to participate. In the case of adults with CP, their parents or legal tutors provided written informed consent, and participants verbalized willingness to participate. The study was approved by the Ethics Committee of the Regional Government of the Balearic Islands.

Cerebral Palsy Assessment

Information about age, type of cerebral palsy, and orthopedic impairments in CP participants was obtained from their health history. The cognitive level of participants with CP was determined by psychologists from the specialized centers by using standardized neuropsychological tests (Wechsler Adult Intelligence Scale-Revised, Wechsler Intelligence Scale for Children-Revised, and Columbia Mental Maturity Scale). These tests were shown to be valid and reliable in neurological populations and have been previously used to assess cognitive functioning in persons with CP [11].

The level of motor impairment was determined by the Gross Motor Function Classification Scale (GMFCS) [12] at the time of the interview. Table 1 displays the clinical characteristics of participants with CP within each age group.

Table 1 Clinical characteristics of persons with cerebral palsy (N = 86) for each age group

Clinical Variable	Children (N = 27)	Adolescents (N = 24)	Young Adults (N = 35)
Type of cerebral palsy			
Bilateral spastic	19	17	20
Unilateral spastic	1	1	2
Diskinetic	4	5	3
Ataxic	2	1	6
Mixed	1	0	4
Motor impairment (GMFCS)			
Level 1	2	3	8
Level 2	5	2	3
Level 3	4	7	3
Level 4	3	3	4
Level 5	13	9	17
Orthopedic impairment			
None	18	9	0
Hip sub-dislocation	7	6	10
Equinus	0	1	9
Scoliosis	2	8	16
Cognitive impairment			
None	7	10	7
Mild	5	2	3
Moderate	2	1	6
Severe	13	11	19

Number of persons classified according with type of cerebral palsy, orthopedic, cognitive, and motor impairment (following the Gross Motor Function Classification Scale [GMFCS]).

Pain-Related Questionnaires

Data about pain and quality of life were collected using a semi-structured interview. Augmentative communication devices and information from parents and caregivers were used as needed to facilitate data collection in subjects with communication difficulties. In addition, parents of all participants with CP completed the same written questions at home, unless they asked to do it in a face-to-face interview. Data from participants with CP who were unable to self-report (N = 43) were completed using their parents' data. This procedure has been used successfully in previous studies [2,4].

Pain was measured by using the following information from the interview:

1. whether they were experiencing chronic pain or not (yes/no response);
2. how many painful clinical treatments, such as surgery and stretching, did they receive;
3. ratings of current and worst pain in the last week by using a 11-point scale (0 = no pain, 10 = unbearable pain); and

4. the location of painful body regions by using a drawing of the human figure, and pain intensity ratings at each location by using a 4-point numerical scale (0 = no pain; 1 = mild; 2 = moderate; 3 = severe) (QL07/00 Pediatric Pain Questionnaire) [13]. Four pain scores were computed by dividing the sum of pain intensity ratings by the number of painful sites for each of the following body locations: head, upper limbs (shoulders, arms, elbows, hands), lower limbs (legs, hips, knees, ankles), and back. Pain scores were set to 0 in all participants with no pain.

The cerebral palsy quality of life (CP-QOL) questionnaire for children [14] was administered to evaluate subjective feelings (ranging from 1 = very sad to 9 = very happy) during several situations grouped in five areas: *social well-being and acceptance, functioning, participation and physical health, emotional well-being and self-esteem*, and *pain*. We decided to use this questionnaire for all the participants regardless of age to make data about quality of life comparable. The CP-QOL questionnaire was also completed by healthy volunteers, except those questions directly related to CP.

Assessment of Touch Sensitivity

Detection thresholds for mechanical stimuli were bilaterally measured at nine body locations (cheek, lip, ventral part of the lower arm, dorsum of the hand, thenar eminence, distal phalanx of the index finger, thoracic back, dorsum of the foot, calf of the leg) in a subgroup of participants (63 persons with cerebral palsy and 34 healthy controls). For this purpose, a kit of von Frey monofilaments (Somedic Sales AB, Sweden) consisting of 17 nylon hairs with increasing diameters (0.14–1.01 mm), constant lengths, and nominal force ranging from 26 mg to 110 g (manufacturer's data) were used. They were applied by pressing the filament at a 90° angle against the skin until it was bent. The filament was held in place for 1.5 seconds and then removed. Subjects were instructed to answer "yes" when a touch stimulus was perceived. After the task was explained, subjects were asked to wear a sleeping eye mask, and some practice trials were given to familiarize them with the assessment procedure. The task began with a randomly selected filament applied to one testing site. When a positive response to the stimulus was obtained, the same filament was applied two more times. If the touch sensation was positively felt in three consecutive trials, a thinner filament was applied to the testing site; if one negative response was given, a thicker filament was used. Null stimuli were also included to detect false positive responses. Responses with a delay greater than 3 seconds were considered as incorrect. Thus, the detection threshold for mechanical stimuli at one specific body location was defined as the lowest pressure perceived by the subject in three consecutive trials. The order for testing the 18 body locations was varied across the subjects, with the only restriction that the two sides of one body location were not assessed consecutively. An average touch sensitivity score was computed considering all body locations.

Statistical Analyses

Group differences on the presence of chronic pain and the number of painful clinical treatments were tested using chi-square and Mann–Whitney tests, respectively. Differences on pain reports (presence of chronic pain, number of painful clinical treatments, current and worst pain intensity, and pain scores at four body locations), touch sensitivity, and quality of life scores were tested by using analyses of variance (ANOVAs) with the between-subject factors GROUP (CP vs healthy controls) and AGE (children vs adolescents vs young adults). In the case of pain scores, an additional within-subjects factor BODY LOCATION (head vs upper limbs vs lower limbs vs back) was included to examine the spatial distribution of pain. ANOVA results were adjusted using Bonferroni corrections for post hoc comparisons and Greenhouse–Geisser corrections for the violation of sphericity assumptions. Pearson correlations were used to examine the relationship between pain reports, touch sensitivity, and age in CP participants and healthy controls. Finally, multiple regression analyses were used to test the contribution of age and quality of life to the current pain intensity in persons with CP and healthy controls.

Results

Subjective Pain Reports

The presence of chronic pain, defined as current pain lasting more than 3 months, was significantly more frequent in participants with CP (45.31%) than in healthy controls (18.40%) (chi-square = 15.37, $P < 0.001$). In addition, participants with CP underwent more painful clinical treatments than healthy controls (Mann–Whitney $U = -4.92$, $P < 0.001$). The univariate ANOVA on current pain intensity yielded a significant GROUP × AGE interaction effect (F[2,205] = 4.40, $P < 0.05$), indicating that current pain intensity was differentially modulated by age in participants with CP and healthy controls. Post hoc comparisons revealed that children with CP reported more enhanced pain intensity than healthy children ($P < 0.05$), whereas no group differences were observed in adults or adolescents. Furthermore, post hoc comparisons indicated that age-related differences on current pain intensity appeared in healthy controls (ps < 0.01) but not in participants with CP (Figure 1).

The ANOVA on worst pain intensity revealed a significant main effect of AGE (F[2,205] = 5.74, $P < 0.01$), indicating that in general, adults reported more pain than children ($P < 0.01$). In addition, the ANOVA on the number of painful locations showed significant main effects of AGE (F[2,205] = 6.23, $P < 0.01$) and GROUP (F[1,205] = 32.1, $P < 0.001$), indicating that persons with CP reported more painful locations than healthy controls ($P < 0.01$) and that adults had more painful locations than children ($P < 0.01$).

The spatial distribution of pain scores at several body locations for CP participants and healthy controls within
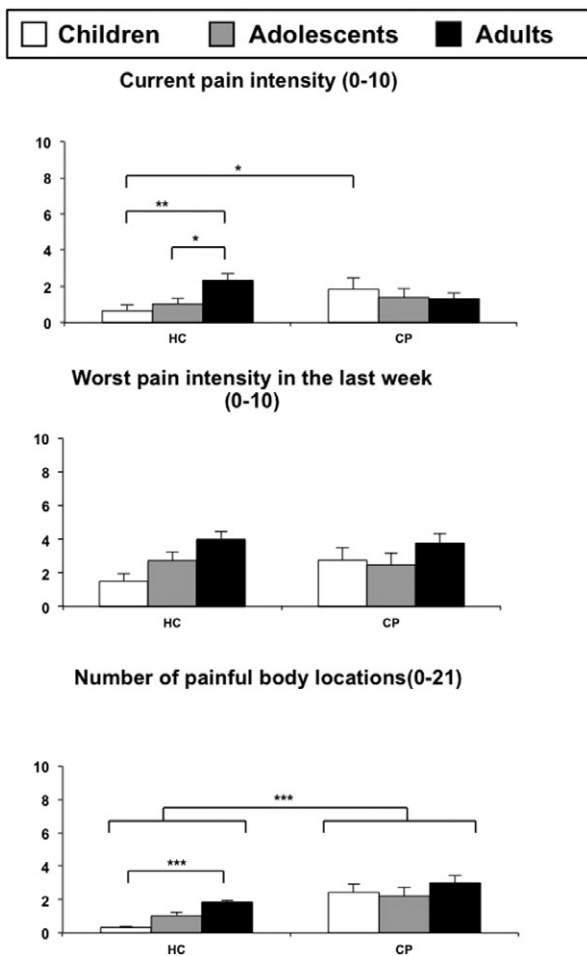
Figure 1 Pain ratings and number of painful body locations in persons with cerebral palsy (CP) and healthy controls (HC) for three age groups: children (6–10 years), adolescents (11–17 years), and young adults (18–30 years). Current and worst pain intensities were measured by using an 11-point scale (0 = no pain, 10 = unbearable pain). Asterisks indicate significant differences on post hoc comparisons (significance level: $*P < 0.05$, $**P < 0.01$, $***P < 0.001$).

each age group is displayed in the upper panel of Figure 2a. The multivariate ANOVA of these scores revealed that pain intensity was significantly higher in persons with CP than in healthy controls (GROUP main effect: $F[1,184] = 17.69$, $P < 0.001$), higher in young adults than in adolescents and children (AGE main effect: $F[2,184] = 3.86$, $P < 0.01$), and higher in lower limbs than in the rest of body locations (BODY LOCATION main effect: $F[3,552] = 19.19$, $P < 0.001$). Moreover, a significant BODY LOCATION $\times$ GROUP interaction effect ($F[3,552] = 13.02$, $P < 0.001$) was found, indicating that

differences on pain intensity appeared on specific body locations. Post hoc comparisons revealed that CP participants reported more enhanced pain scores than healthy controls on back ($P < 0.05$), lower limbs ($P < 0.001$), and upper limbs ($P < 0.01$) but not on head pain (Figure 3). Moreover, lower limb pain was more intense than both upper limb ($P < 0.001$) and head pain ($P < 0.001$) in CP participants, whereas back pain was more intense than both upper ($P < 0.001$) and lower limb pain ($P < 0.05$) in healthy controls.

Touch Sensitivity

Figure 2b displays a topographical distribution of touch sensitivity thresholds on the nine body locations (cheek, lip, ventral part of the lower arm, dorsum of the hand, thenar eminence, distal phalanx of the index finger, thoracic back, dorsum of the foot, calf of the leg) in participants with CP (N = 63) and healthy controls (N = 34) for each age group. Due to the small sample sizes, a mean threshold index was calculated by averaging the threshold values across all nine body locations. The ANOVA on the average thresholds revealed a significant interaction effect between GROUP and AGE ($F[2,91] = 5.1$, $P < 0.01$) and a GROUP main effect ($F[1,91] = 8.94$, $P < 0.01$). Post hoc comparisons indicated that CP adults and young adults were less sensitive to touch than healthy adults and young adults (ps < 0.01). Moreover, post hoc comparisons also revealed that healthy children had more reduced touch sensitivity than healthy adults ($P < 0.05$) (Figure 4).

Quality of Life

Figure 4 displays the mean scores on the five domains of the CP-QOL in persons with CP and healthy controls within each age group (children, adolescents, and young adults). Participants with CP and healthy controls differed in all domains of the CP-QOL. In particular, CP reported lower scores than healthy controls in *social well-being and acceptance* (GROUP main effect: $F[1,195] = 11.11$, $P < 0.01$), *participation and physical health* (GROUP main effect: $F[1,195] = 20.26$, $P < 0.001$), *emotional well-being and self-esteem* (GROUP main effect: $F[1,195] = 16.31$, $P < 0.001$), and *functioning* (GROUP main effect: $F[1,195] = 21$, $P < 0.001$). Moreover, CP participants had higher scores in the domain *Pain* (GROUP main effect ($F[1,195] = 8.64$, $P < 0.01$) than healthy controls. In addition, main effects of AGE were found in *participation and physical health* ($F[2,195] = 12.03$, $P < 0.001$) and *emotional well-being and self-esteem* scores ($F[2,195] = 22.46$, $P < 0.001$), indicating that children had higher scores than adolescents and young adults in both groups (all ps < 0.05). No significant interaction effects between GROUP and AGE were yielded in any of the CP-QOL domains (Figure 5).

Relationship Between Pain Reports, Age, and Touch Sensitivity

Significant positive correlations were found between different pain reports (current and worst pain intensity,
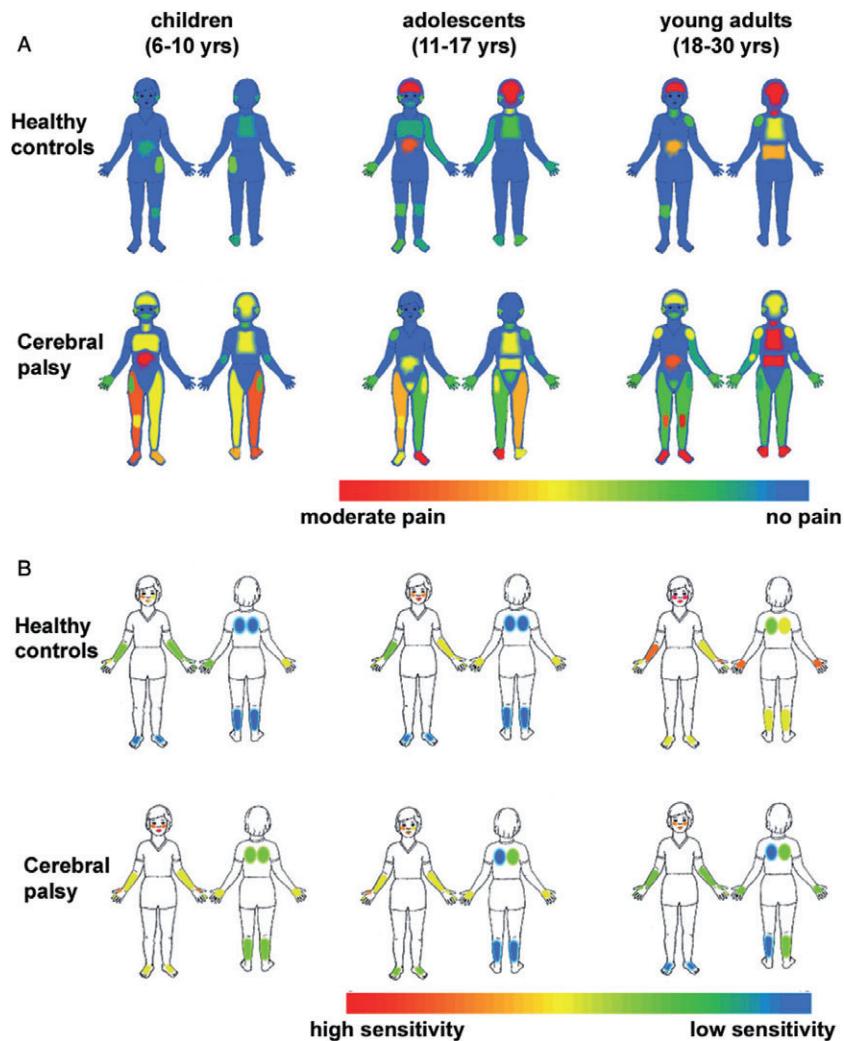
Figure 2 Topographical distribution of pain intensity scores and touch sensitivity thresholds on several body locations. (Panel A) Pain was obtained from participants' self-reports by rating the intensity of pain sensations at each body region with a 4-point numerical scale (0 = pain, 1 = mild, 2 = moderate; 3 = severe). The color-based scale ranges from 0 (when all the people reported no pain) to 1 (equivalent to moderate pain). (B) Touch sensitivity was measured bilaterally applying von Frey monofilaments at nine body locations (cheek, lip, ventral part of the lower arm, dorsum of the hand, thenar eminence, distal phalanx of the index finger, thoracic back, dorsum of the foot, calf of the leg).

number of painful locations, head pain score, back pain score) and age in healthy controls, whereas no significant correlation were found between pain reports (except for upper limb pain) and age in participants with CP (Table 2). Moreover, worst pain intensity was negatively correlated with touch sensitivity thresholds in healthy controls, indicating that enhanced pain was associated with enhanced touch sensitivity. By contrast, head, lower limb, and back pain scores were positively correlated with touch sensitivity thresholds in participants with CP, indicating that enhanced pain was associated with reduced touch sen-

sitivity. Finally, back pain was positively correlated with the number of orthopedic problems in CP.

To further analyze the contribution of age and psychosocial variables to current pain in healthy controls and individuals with CP, multiple regression analyses were performed separately for each group of participants using *Current pain intensity* as the dependent variable and age and quality of life scores as predictor variables. The analyses showed that different predictors accounted for a significant proportion of the variance in individuals with CP
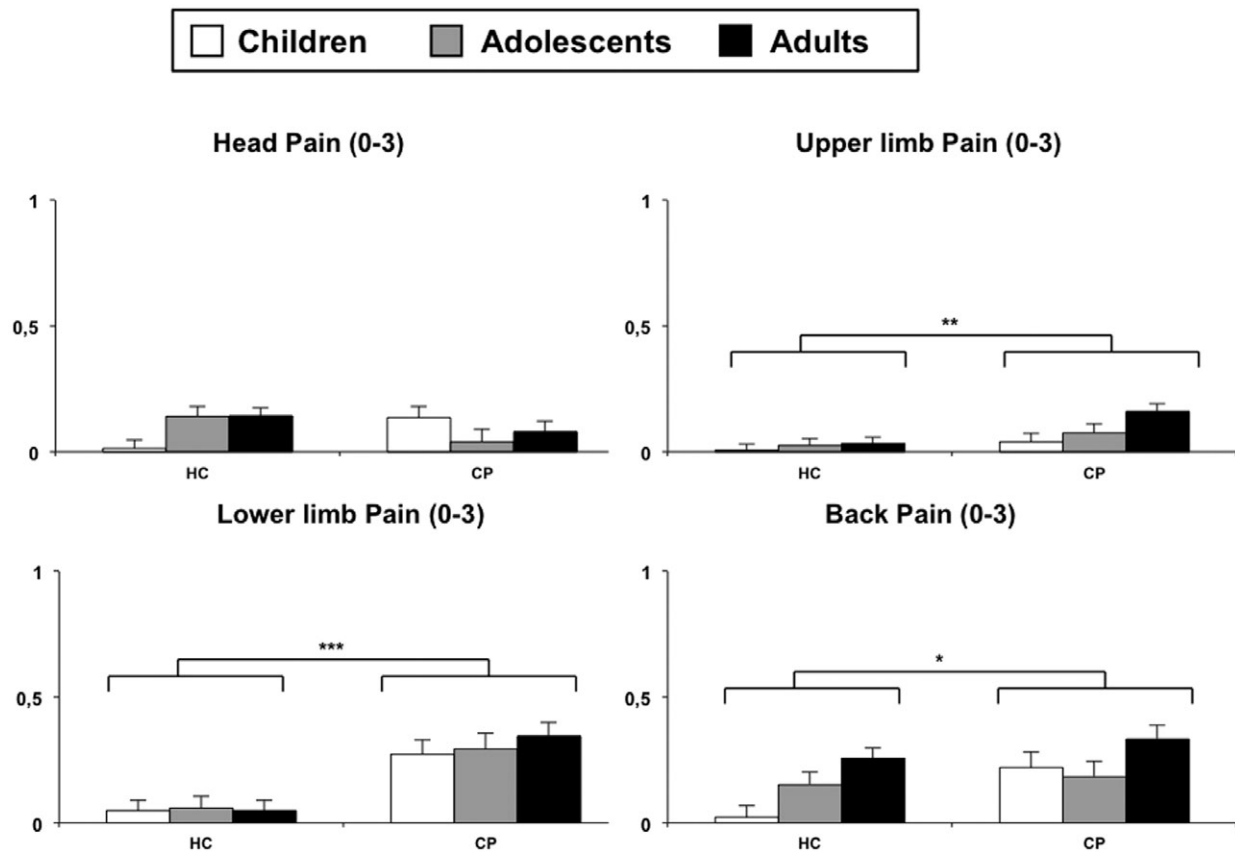
Figure 3 Pain scores on four body locations in persons with cerebral palsy (CP) and healthy controls (HC) for three age groups: children (6–10 years), adolescents (11–17 years), and young adults (18–30 years). Pain scores were computed by dividing the sum of pain intensity ratings by the number of painful sites for each of the following body locations: head, upper limbs (shoulders, arms, elbows, hands), lower limbs (legs, hips, knees, ankles), and back. Asterisks indicate significant differences on post hoc comparisons (significance level: *P < 0.05, **P < 0.01, ***P < 0.001).

($r = 0.447$, F[2,83] = 10.37, $P < 0.001$) and healthy controls ($r = 0.238$, F[1,113] = 7.39, $P < 0.01$). In persons with CP, two CP-QOL subscales (*Functioning* and *Emotional well-being and self-esteem*) were significant predictors of *Current pain intensity*, whereas *age* was the best predictor of pain intensity in healthy controls (Table 3).

Discussion

The major aim of the present study was to analyze age-related differences on pain and touch sensitivity in persons with CP and healthy controls. Basically, we found that participants with CP reported more pain, lower touch sensitivity, and more reduced quality of life than healthy controls. Moreover, it was observed that differences on pain reports and touch sensitivity were mediated by age in healthy controls but not in persons with CP. In addition, analyses of the relationship between pain and touch sensitivity revealed that increased pain intensity was associated with increased average touch sensitivity in healthy controls, whereas increased ratings of head, lower limb, and back pain were associated with reduced touch sensitivity in participants with CP.

In the present study, 43% of participants with CP experienced pain as chronic and underwent more painful clinical treatments than healthy controls. These findings are in agreement with previous reports indicating that around 60% of persons with CP experience recurrent pain of a moderate-to-severe intensity on a daily or weekly basis that significantly interferes with daily activities [2,4,15–17]. Moreover, our data suggest that pain reported by participants with CP was significantly above the prevalence rate of pain among the general population. However, contrasting with the extensive data about pain in adults, little is known about pain characteristics among children and adolescents. To date, almost all epidemiological studies have focused on the presence of specific pain syndromes
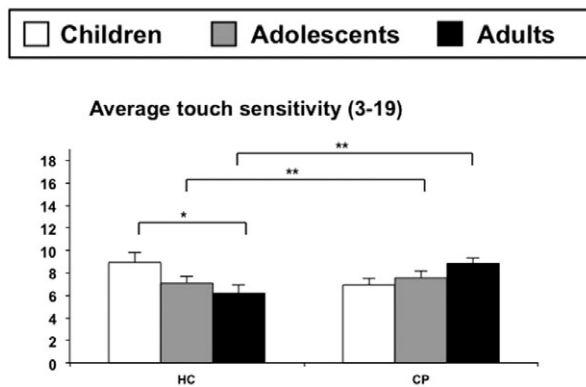
Figure 4 Average touch sensitivity in persons with cerebral palsy (CP) and healthy controls (HC)for three age groups: children (6–10 years), adolescents (11–17 years), and young adults (18–30 years). Touch sensitivity was computed as the average threshold of nine body locations (cheek, lip, ventral part of the lower arm, dorsum of the hand, thenar eminence, distal phalanx of the index finger, thoracic back, dorsum of the foot, calf of the leg). Asterisks indicate significant differences on post hoc comparisons (significance level: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).

(e.g., juvenile chronic arthritis, knee pain, fibromyalgia, low back pain, cancer pain, migraine, headache), rather than on specific clinical manifestations of chronic pain. In this context, our data on the prevalence of pain among healthy children and adolescents seem to be in agreement with previous population-based surveys. Thus, recent cross-sectional studies revealed that around 25–40% of school-children reported chronic pain [18,19], although only 5.1% had moderate or severe pain problems. In addition, according with other epidemiological surveys of the general population [18–21] our data show a significant enhancement of pain with increased age among healthy controls. A further survey among children (5–16 years of age) with different chronic diseases (arthritis, cancer, enuresis, and headache) and healthy showed that presence of chronic pain differed depending on the health condition, with the lowest rates (4–7%) in healthy and children with enuresis or headache and the highest rates (78%) in children with arthritis [21]. Thus, it seems that chronic pain in CP appears to have similar rates than in other chronic diseases.

A further relevant finding of the present study was that pain and quality of life were not influenced by age in CP, but significant age-related differences appeared in healthy controls. We observed that healthy children reported lower pain scores and a better quality of life compared with healthy young adults. In contrast, the three age groups of participants with CP did not differ in pain ratings (except for upper limb pain) or quality of life. Moreover, age was the best predictor of pain intensity in healthy controls but not in participants with CP. These findings are in agreement with previous surveys in healthy adult samples indicating that the prevalence of chronic pain increases with aging and that age influences pain perception [16,17,22]. Moreover, our data further suggest that the influence of age on pain would extend to children and adolescents among the general population. Pain in CP appears to be a relevant phenomenon from an early age, showing no age-related changes over the life span. Therefore, it seems that the presence of pain should be specifically addressed in rehabilitation programs for children and adolescents with CP.

Interestingly, our findings showed that age-related changes in pain perception were mirrored by age-related changes in touch sensitivity (detection of light pressure against the skin using the von Frey monofilaments) in healthy controls but not in subjects with CP. Moreover, enhanced persistent pain was associated with reduced touch sensitivity in healthy controls, but a reduced sensitivity among individuals with CP was observed. In addition, significant differences on touch sensitivity were found only between healthy controls and persons with CP in young adults and adolescents but not in children. These findings are in agreement with previous reports indicating that touch and pressure sensitivity are less impaired in children with CP than other measures of sensitivity such as the two-point discrimination [23]. Our data extend those findings to show that touch sensitivity is impaired in young adults and adolescents with CP but not in children compared with age-matched healthy controls. Increased sensitivity to non-noxious stimulation (allodynia) measured by von Frey monofilaments is also a characteristic of patients suffering from chronic pain, particularly of those with neuropathic pain [24]. In this sense, the positive relationship observed between pain and touch sensitivity in healthy controls might be the result of plastic changes associated with the persistence of pain over time [17]. In contrast, reduced touch sensitivity together with enhanced pain observed in CP may indicate the existence of different psychophysiological mechanisms for the maintenance of pain. The implications of these age-related changes in touch sensitivity and pain for the development of chronic pain in healthy people and in persons with CP should be addressed in future studies using several measures of experimental pain sensitivity.

Our finding of a high level of pain compared with healthy controls is also of special importance because it has been suggested that pain reports in childhood and early adolescence could be associated with increased pain [25] and affective disorders in adulthood [26]. Moreover, repeated painful experiences during periods of neurological development may cause relevant changes in pain thresholds and tolerance throughout a person's lifetime [27]. In this sense, it has been suggested that the regular participation of children with CP in chirurgic and rehabilitation procedures (stretching, electrical stimulation, functional mobility
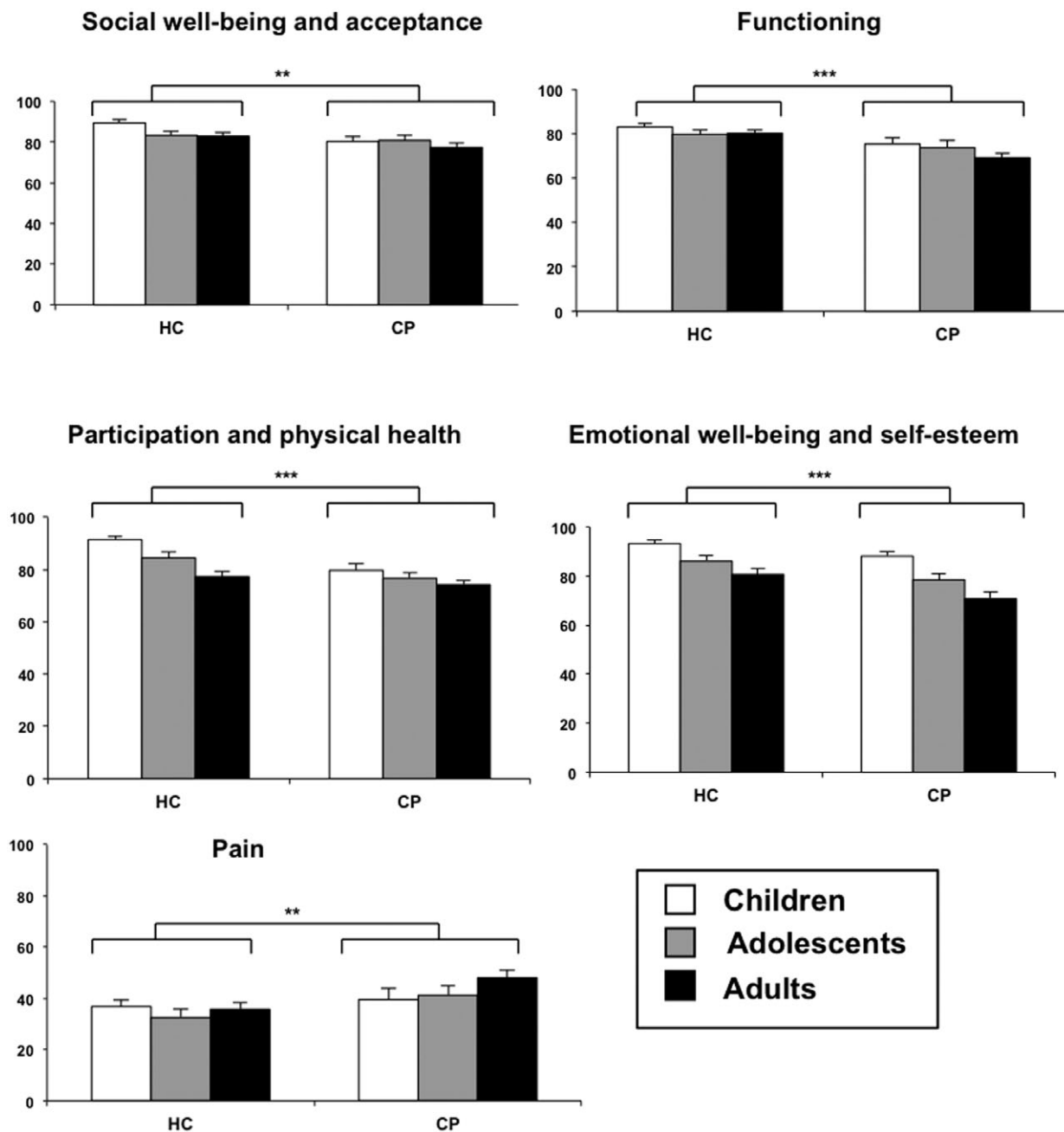
Figure 5 Scores on the cerebral palsy quality of life (CP-QOL) questionnaire in persons with CP and healthy controls (HC) for three age groups: children (6–10 years), adolescents (11–17 years), and young adults (18–30 years). Asterisks indicate significant differences on post hoc comparisons (significance level: $*P < 0.05$, $**P < 0.01$, $***P < 0.001$).

training, splinting and orthotic fabrication, serial casting, training for use of adaptive equipment, and utilization of standing frames and other positioning devices) could be associated with a high prevalence of pain [25]. Furthermore, it has been noted that parents of children with CP identified assisted stretching as the most frequent painful

activity of daily living [28] and that one of the most salient negative memories of childhood in adults with CP is pain related to stretching and bracing in physical therapy [29]. Thus, it appears that ongoing rehabilitation efforts would lead to increasing anxiety, fear, frustration, withdrawal, or distress about these interventions and facilitate the

Table 2 Relationship between several measures of pain and age, touch sensitivity, and motor impairments in participants with cerebral palsy and healthy controls

	Current Pain Intensity	Worst Pain Intensity	Number of Painful Locations	Head Pain	Upper Limb Pain	Lower Limb Pain	Back Pain
Persons with cerebral palsy (N = 86)							
Age	−0.109	0.087	0.102	−0.035	0.292*	0.096	0.150
Touch sensitivity threshold	0.155	0.164	0.117	0.317*	0.159	0.353**	0.299*
Motor level (GMFCS)	0.087	0.001	−0.194	−0.225	−0.060	−0.122	−0.150
Number of orthopedic problems	0.041	−0.197	0.097	0.114	0.325	0.035	0.434*
Healthy controls (N = 115)							
Age	0.238**	0.230***	0.457***	0.309**	0.120	0.030	0.336**
Touch sensitivity threshold	−0.163	−0.218*	−0.331	−0.227	−0.136	−0.107	−0.212

$* \ P < 0.05, \ ** \ P < 0.01, \ *** \ P < 0.001.$

GMFCS = gross motor function classification scale.

Current and worst pain intensities were measured by using an 11-point scale (0 = no pain, 10 = unbearable pain). The head, upper/lower limb, and back pain scores were obtained by using a 4-point scale (0 = no pain; 1 = mild; 2 = moderate; 3 = severe) (upper limb pain scores were computed by averaging the pain scores for shoulders, arms, elbows, and hands; lower limb pain scores were computed by averaging the pain scores for legs, hips, knees, and ankles).

Table 3 Multiple regression predictors of current pain intensity in persons with cerebral palsy and healthy controls

Predictors	Beta	Adj R2	R2
(a) Individuals with cerebral palsy (N = 86)			
Age	−0.104		
Social well-being and acceptance	−0.021		
Functioning	−0.502**		
Participation and physical health	−0.233		
Emotional well-being and self-esteem	0.296*		
Pain	0.159		
		0.181	0.200
(b) Healthy controls (N = 125)			
Age	0.238*		
Social well-being and acceptance	−0.002		
Functioning	−0.006		
Participation and physical health	−0.033		
Emotional well-being and self-esteem	−0.063		
Pain	−0.076		
		0.049	0.057

$* \ P < 0.01, \ ** \ P < 0.001.$

establishment and maintenance of pain memories [19,30]. In this sense, the present study highlights the importance of considering the presence of pain at very early ages in CP.

Nevertheless, our study has some limitations that should be taken into account for the interpretation of the results. Although our sample of persons with CP was selected from educational and occupational settings in our community, it is small, and the response rate was low. Moreover, it is noteworthy that the selected sample displays the different characteristics concerning motor and cognitive impairments and the type of CP compared with other epidemiological studies. The use of questionnaires, although adequate for this explorative purpose, has some important methodological bias such as the use of the same questionnaires by persons with diverse cognitive and developmental abilities that may cause some distortions. The use of pediatric questionnaires in an adult population and the lack of the proven validity of some instruments in healthy samples, such as the CP-QOL measure, may have introduced some methodological biases in the study. Moreover, the use of self and surrogate pain reports may have decreased the reliability of the data. Finally, the cross-sectional design of the present study represents a further limitation. Although our study does not provide information about how pain experience changes over time in CP, it lays a scientific basis for the

implementation of a longitudinal design and it guides the selection of appropriate outcome measures for future studies.

In conclusion, it appears that pain experience in CP participants was not influenced by age in a similar way as it happened in the healthy population. This suggests that different psychosocial and psychophysiological mechanisms may be involved in the maintenance of pain over the life span.

Competing Interests

The authors declare that they have no competing interests.

Author's Contribution

PM and IR conceived of the study, participated in its design and coordination. IR, IC, and PM performed the statistical analysis and executed the drafting of the manuscript. IR carried out the interviews and sensitivity tests.

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References

1 Berrin SJ, Malcarne VL, Varni JW. Pain, fatigue, and school functioning in children with cerebral palsy: A path-analytic model. J Pediatr Psychol 2007;32:330–7.

2 Breau LM, Camfield CS, McGrath PJ, Finley GA. The incidence of pain in children with severe cognitive impairments. Arch Pediatr Adolesc Med 2003;157:1219–26.

3 Engel JM, Petrina TJ, Dudgeon BJ, McKearnan KA. Cerebral palsy and chronic pain: A descriptive study of children and adolescents. Phys Occup Ther Pediatr 2005;25:73–84.

4 Tervo RC, Symons F, Stout J, Novacheck T. Parental report of pain and associated limitations in ambulatory children with cerebral palsy. Arch Phys Med Rehabil 2006;87:928–34.

5 White-Koning M, Arnaud C, Dickinson HO, et al. Determinants of child-parent agreement in quality-of-life reports: A European study of children with cerebral palsy. Pediatrics 2007;120:804–14.

6 Bjornson KF, Belza B, Kartin D, Logsdon R, McLaughlin J. Self-reported health status and quality of life in youth with cerebral palsy and typically developing youth. Arch Phys Med Rehabil 2008;89:121–7.

7 Schmelzle-Lubiecki BM, Campbell KA, Howard RH, Franck L, Fitzgerald M. Long-term consequences of early infant injury and trauma upon somatosensory processing. Eur J Pain 2007;11:799–809.

8 Sanger TD, Kukke SN. Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. J Child Neurol 2007;22(3):289–93.

9 Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Joint-position sense and kinesthesia in cerebral palsy. Arch Phys Med Rehabil 2009;90(3):447–53.

10 Riquelme I, Montoya P. Developmental changes in somatosensory processing in cerebral palsy and healthy individuals. Clin Neurophysiol 2010;121:1314–20.

11 Ito J, Araki A, Tanaka H, Tasaki T, Cho K. Intellectual status of children with cerebral palsy after elementary education. Pediatr Rehabil 1997;1:199–206.

12 Palisano R, Rosenbaum P, Walter S, et al. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997;39:214–23.

13 Varni JW, Burwinkle TM, Seid M. The PedsQL™ as a pediatric patient-reported outcome: Reliability and validity of the PedsQL™ Measurement Model in 25,000 children. Expert Rev Pharmacoecon Outcomes Res 2005;5:705–19.

14 Waters E, Davis E, Mackinnon A. Psychometric properties of the quality of life questionnaire for children with CP. Dev Med Child Neurol 2007;49:49–55.

15 Houlihan CM, O'Donnell M, Conaway M, Stevenson RD. Bodily pain and health-related quality of life in children with cerebral palsy. Dev Med Child Neurol 2004;46:305–10.

16 Gibson SJ, Helme RD. Age-related differences in pain perception and report. Clin Geriatr Med 2001;17:433–56.

17 Gibson SJ, Farrell M. A review of age differences in the neurophysiology of nociception and the perceptual experience of pain. Clin J Pain 2004;20:227–39.

18 Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. Pain in children and adolescents: A common experience. Pain 2000;87:51–8.

19 Huguet A, Miró J. The severity of chronic pediatric pain: An epidemiological study. J Pain 2008;9:226–36.

20 Martin AL, McGrath PA, Brown SC, Katz J. Anxiety sensitivity, fear of pain and pain-related disability in children and adolescents with chronic pain. Pain Res Manag 2007;12:267–72.

21 McGrath PA, Speechley KN, Seifert CE, et al. A survey of children's acute, recurrent, and chronic pain: Validation of the pain experience interview. Pain 2000;87:59–73.

22 Lautenbacher S, Kunz M, Strate P, Nielsen J, Arendt-Nielsen L. Age effects on pain thresholds, temporal summation and spatial summation of heat and pressure pain. Pain 2005;115:410–8.

23 Krumlinde-Sundholm L, Eliasson AC. Comparing tests of tactile sensibility: Aspects relevant to testing children with spastic hemiplegia. Dev Med Child Neurol 2002;44:604–12.

24 Keizer D, Fael D, Wierda JM, van Wijhe M. Quantitative sensory testing with Von Frey monofilaments in patients with allodynia: What are we quantifying? Clin J Pain 2008;24:463–6.

25 Brattberg G. Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 2004;8:187–99.

26 Campo JV. Coping with ignorance: Exploring pharmacologic management for pediatric functional abdominal pain. J Pediatr Gastroenterol Nutr 2005;41:569–74.

27 Mitchell A, Boss BJ. Adverse effects of pain on the nervous systems of newborns and young children: A review of the literature. J Neurosci Nurs 2002;34:228–36.

28 McKearnan KA, Kieckhefer GM, Engel JM, Jensen MP, Labyak S. Pain in children with cerebral palsy: A review. J Neurosci Nurs 2004;36:252–9.

29 Kibele A. Occupational therapy's role in improving the quality of life for persons with cerebral palsy. Am J Occup Ther 1989;43:371–17.

30 Turnquist KM, Engel JM. Occupational therapists' experiences and knowledge of pain in children. Phys Occup Ther Pediatr 1994;14:35–51.

Manuscrito:

Physical therapist actuation on the experience of pain in cerebral palsy

PHYSICAL THERAPIST ACTUATION ON THE EXPERIENCE OF PAIN IN CEREBRAL PALSY

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ABSTRACT

Background: Pain seems to be an important problem for individuals with cerebral palsy. In addition to pain associated to spasticity and musculoskeletal problems, persons with cerebral palsy are often exposed to physical therapy techniques which may cause or relieve pain. ***Objectives***: 1) To compare the perception of pain between persons with cerebral palsy and their physical therapists and 2) to examine the repercussion of the physical therapist's actuation in pain suffered by cerebral palsy individuals. ***Design***: A cross-sectional descriptive design was used. ***Methods***: Semi-structured interviews about pain characteristics (intensity, location and interference), pain intensity and relief produced by sanitary procedures, behaviors used to express pain and actuations against pain were answered by persons with cerebral palsy (n=128; communicative cerebral palsy=50, non-communicative cerebral palsy=78) and their physical therapists (n=18). Moreover, a pain report using a 11-point VAS scale was obtained from communicative CP and their physical therapists during the performance of hamstring stretching and passive joint mobilization. ***Results***: Thirty-six percent of individuals with cerebral palsy experienced pain of moderate intensity, mostly located in lower limbs, which interfered with physical exercise. Moreover, frequent sanitary procedures as surgery, botulinum toxin A injections or stretching are reported as causes of moderate pain. Analgesic physical therapy techniques are reported as at least moderately useful to relieve pain. Pain is mostly expressed by verbal reports, facial and vocal signs and changes in the body movements. The more frequent strategies used in front of a painful episode were avoiding painful stimulus, treating with pharmacology of physical therapy techniques and informal care. No significant differences were found between persons with cerebral palsy and their physical therapists regarding the main aspects which define pain. No significant differences were found between the reports of communicative children and their physical therapists, or between physical therapists' reports of communicative and non-communicative persons with cerebral palsy. ***Conclusions***: Some physical therapy techniques may produce pain in persons with cerebral palsy. Physical therapists seem able to recognize the behaviors used to express pain by persons with cerebral palsy despite its level of verbal capacity. Although physical therapists perform different actuations to relief pain when it is detected, no formal pain assessment or treatment seems to be carried out. Standardized pain assessment and treatment for cerebral palsy remains an important clinical and research challenge.

Pain in neurological patients may be frequently underestimated and, therefore, poorly treated. This risk is particularly important in individuals who have impaired cognitive ability to describe their pain (McGrath et al., 1998). Persons with cerebral palsy (CP) are at increased risk of experiencing acute, chronic and procedural pain. As well as pain experimented by the general population (Hunt et al., 2003; Carter et al., 2002), CP often experience ongoing pain from a variety of disabilities such as dislocated hips, muscle spam, gastro-oesophageal reflux and back and limbs pain (Jóźwiak et al., 2010; Doralp & Bartlett, 2010; Russo et al., 2008; Castle et al., 2007; Gallien et al., 2007; Jahnsen et al., 2004; Engel et al., 2003; Nolan et al., 2000; Schwartz et al., 1999). CP may also require surgical interventions and cope with the sore caused by handling, immobility and poorly fitting aids and equipment (Lannin et al., 2008; Hunt et al., 2003; Carter et al., 2002) and from early childhood they are exposed to repeated painful sanitary procedures (Brattberg G., 2004; McKearnan et al., 2004; Carter et al., 2002; Hadden &Von Baeyer, 2002; Kibele A., 1999).

Optimal pain management depends on accurate assessment of the person's behavior. Verbal self-report has historically been characterized as the "gold standard" technique in pain assessment (McGrath PA., 1987). Communication difficulties make persons with neurological impairments especially vulnerable to poor pain management. In these situations, pain might be inadequately treated because it is not adequately recognized (McGrath et al., 1998). However, CP express discernible pain behaviors regardless of cognitive or language ability (Hadden & von Baeyer, 2005). Anand & Craig (1996) proposed that the behavioral alterations caused by pain in non-verbal populations should be recognized as forms of self-report and that attention to these behavioral responses would help to optimize pain management. Nevertheless, typical pain behaviors such as moaning of facial changes may not actually reflect pain in CP, whilst other idiosyncratic behaviors may be pain related (Nolan et al., 2000; Breau et al., 2000; McGrath et al., 1998).

Considering that some physical therapy procedures, as stretching or manipulation to increase the range of movement, are reported as the most painful among the health interventions in CP (Brattberg G., 2004; McKearnan et al., 2004; Hadden &Von Baeyer, 2002; Kibele A., 1999) and that these procedures are performed almost in a daily basis, it is important to know physical therapist perception of CP's pain characteristics. Despite the agreement between children and health professionals reports of pain has been widely studied in general health settings or during a hospitalization

stay, few studies have focused in professionals with a long contact with the CP, as the physical therapists. However, pain in CP is a common important concern both for CP and physical therapists (Vargus-Adams & Martin, 2010; Hilberink et al., 2008). The objective of this study is to compare the agreement in the perception of CP's pain between CP and their physical therapists and to examine the repercussion of the physical therapist's actuation in the pain experience of persons with CP.

METHODS

Participants

In the study participated 128 children, adolescents and young adults with cerebral palsy (mean age=18.99 yrs, range: 6-30 yrs, SD=12.77; 45 females), and their physical therapists (n=18) recruited from several educational and occupational centers of Majorca (Spain). Inclusion criteria were: (1) aged from 4 to 30 years and (2) cognitive level that allows the person to understand and answer questions about their medical and psychological health status. Lower age was set in 4 years according to the findings of previous research which assures that these children can accurately provide pain self-reports[16]. Subjects were not excluded based on specific communication difficulties. Augmentative communication devices were used as needed to facilitate data collection. Those subjects non able to communicate even with augmentative communication devices, were classified as "non-communicative CP".

Data from physical therapists of non-communicative CP (n=78) were also collected, in order to examine possible differences between the perceptions of these adult proxys on the pain of verbally communicative CP (n=50) and non communicative CP.

Type of cerebral palsy and cognitive level was obtained by medical reports. The level of motor impairment was obtained by an experienced physical therapist (I.R.). using the Gross Motor Function Classification Scale (GMFCS) (Palisano et al., 2000) Table 1 displays clinical characteristics of participants with cerebral palsy.

- Please, insert Table 1 about here -

Parents or legal guardians of all subjects participating in the study granted written informed consent according with the Declaration of Helsinki. The study was approved by Ethics Committee of the Regional Government of the Balearic Islands.

Measures

The study participants (communicative PC, n=50, and their physical therapists, n=18) were administered a protocol-based interview with questions about demographic and clinical data and several pain characteristics: intensity, location, amount of pain and relief provided by health procedures, recognition and expression of pain, number of medical consultations referring pain and actuation in front of pain. The interview was designed from the results obtained by Hadden et al. (2002, 2005) about expression of pain in persons with CP and by Engel et al. (2002) about pain treatment in the population with CP.

Pain was measured using several scores: 1) asking subjects during the interview whether they were experiencing chronic pain or not (pain with more than 3 months of duration), 2) assessing current and worst pain in the last week using a 11-point scale and 3) asking for the number of painful body regions using a drawing of a human figure and the intensity of pain sensation at each location (numerical or colour scale: 1 = mild, 2 = moderate; 3= severe) (QL 07/00 Paediatric Pain Questionnaire) (Varni et al., 2002).

Pain in 11 commonly health procedures (stretching, passive mobilizations, massage, assistive standing, assistive walking, assistive sitting, use of splints, personal hygiene, surgery, botulinum toxin A injections and medical assessment) was assessed using a faces-scale in CP and a 11-point scale in physical therapists.

In order to compare the retrospective perception of pain with the current pain caused by health procedures, a 11-point VAS scale was used to obtain the pain report from communicative CP and their physical therapists during the performance of three different physical therapy common techniques: hamstring stretching, passive joint mobilization of foot or hip and balance exercises in a standing position. CP and physical therapists were answering in separated papers and any of them knew the answers of the other person.

Regarding pain relief provided by different health procedures (medication, heat, stretching, massage, splints, ice, ultrasounds, passive mobilization, active exercise, hydrotherapy, exercise in the swimming-pool, TENS, biofeedback, relaxation techniques and psychological treatment) two different variables were scored: intensity of pain relief and duration of pain relief. Intensity of pain was measured with a face-scale or a 11-point scale, while duration of pain was scored in hours, from less than 1 hour to 48 hours. Same face-scale or 11-point scale were used to assess the interference

of pain in daily activities such as physical exercise, school attendance, sleep or leisure activities.

Expression and recognition of pain was asked in open questions and answers were classified using the Non-communicating Children's Pain Checklist-Revised (NCCCP-R) scale domains (vocal, social, facial, activity, body and limbs, physiologic and eating/sleep), plus one domain called "verbal". The psychometric properties of this scale has been reported in the literature (Breau et al., 2002). Also open questions were used to ask for the actuation of physical therapists in front of the CP's pain, classifying the answers in the following categories: nothing, looking for medical advice, assessing the causes, giving medication, using an analgesic physical therapy technique, avoiding the painful stimulus and informal care (distraction, physical contact, reassuring).

Procedure

CP's data were collected in face-to-face interviews at different educational centers. In addition, physical therapists of all participants with cerebral palsy completed the same questionnaires at home in a written way, unless they asked to do it by a personal interview. Physical therapists completed one questionnaire by each of the CP they were treating.

Pain report during the performance of three different physical therapy common procedures (hamstring stretching, passive joint mobilization of foot or hip and balance exercises in a standing position) was obtained from CP and physical therapists, who answered in separated papers, not knowing any of them the answers of the other person. The physical therapy procedure was performed by the CP physical therapist in the same way it would have been performed in the normal treatment.

Data analysis

Study of frequencies and percentages of the CP data was used to report the descriptive data about presence of chronic pain, location of pain and number of medical visits due to pain. Descriptive means and standard deviation were used to obtain the intensity of current and worst pain during the previous week and the interference of pain in daily life activities. Kendall bivariant correlations were used to compare the relationship among the number of painful areas and the intensity of pain with cognitive level and motor impairment.

Descriptive means and standard deviation were used to obtain the intensity of pain and relief caused by health procedures, and duration of relief produced by these procedures. Study of frequencies and percentages of the CP and physical therapists' data was used to report the descriptive results about frequency of use of analgesic techniques and the kind of intervention used by the physical therapists in front of CP pain.

Study of frequencies and percentages of the CP and their physical therapists' data was used to report the descriptive data about kind of expression of pain.

The data of physical therapists' reports for communicative and non-communicative CP was also compared with a non-parametrical test for independent samples (U-Mann Whitney).

To compared the answers form CP and from their physical therapists, absolute values of the differences (CP score vs. physical therapist score) were calculated and tested using paired tests. The mean difference score was standardized by relating this score to the average standard deviation of the CP and physical therapist scores (effect size). The means of the absolute value of the differences between scores were calculated as indicators of agreement (coefficient of agreement). We further defined agreement as occurring when this absolute value was less than or equal to half of the SD of the children's scores (because these had the greatest variability), according to the recognized definition of clinically meaningful difference in domains of quality of life (Norman et al., 2003). This procedure has been used previously in the literature to evaluate agreement between CP and their parents and between CP parents and professionals (White-Koning et al., 2007, 2008).

RESULTS

Response rates to the questionnaire were heterogeneous. The variability of the pathology on each person and of the procedures used in their physiotherapy intervention made response rates vary in the different questions. Thus, responses to the presence and intensity of pain had response rates of 100-75%; responses rates to intensity of pain due to sanitary procedures varied from 76% of stretching to 26% of use of Botulim toxin Type A; and all the responses regarding intensity and duration of relief of health procedures had responses rates lower to 30%. To avoid possible bias, we excluded the domains which presented a response rate minor to 50% from the agreement calculation

and reported them only as frequency percentages. This procedure was also employed for data related to expression and communication of pain, extracted by open questions.

Incidence and characteristics of pain

More than one third of individuals with cerebral palsy (36%, SD=37.5%) experienced chronic pain of moderate intensity, rating the intensity of pain in the previous week with a mean of 3.50 out of 11 (SD=2.78) and the worst pain intensity during the previous week with a mean of 5.95 out of 11 (SD=3.11). Significant agreement was found between CP's estimation of the intensity of pain and the perception of their physical therapists, who rated the presence of pain in a 31% of the CP population (SD=31.2) and scored the intensity of pain during the previous week with a mean of 3.38 out of 11 (SD=1.96) and the worst pain intensity during the previous week with a mean of 6.27 out of 11 (SD=2.24).

Pain was the cause of 40% of the annual medical visits. The mean of painful zones was 3 and were mainly located in lower limbs (27.00% of incidence), abdomen (16.30%) and dorsal spine (12.70%). No significant correlation was found between pain intensity or location and motor impairment. Pain was reported to interfere mostly in activities which required some kind of physical activity, as running (mean of interference=4.27/10), walking (3.85/10) and climbing stairs (3.4/10). Agreement was found between the perception of CP and their physiotherapists regarding the level of interference caused by pain in physical activities.

Pain perception and pain relief of common physical therapy procedures

Physical therapy procedures were considered mildly painful compared with other sanitary interventions commonly applied to CP, with only stretching scoring higher than 4 in the 11-points scale. Pain intensity produced by the most painful procedures is shown in Table 2.

-Please, insert Table 2 about here-

In order to check that the retrospective memory of pain mirrored the actual intensity of pain, an observer scored CPs' pain self-reports and physical therapists' reports during two common physical therapy procedures: hamstring streeching and mobilization of foot or hip. No significant differences were found between the pain

intensity directly scored during the intervention and the intensity of the pain caused by stretching or passive mobilization reported in the questionaires, either in CP (Z(25)=-1.084 and Z(42)=-.446 respectively, both ps>.270) or physical therapists (Z(45)=-2.052 and Z(46)=-1.296 respectively, both ps>250). Agreement was found in the perception of physical therapists and CP in the pain produced by health procedures, both in the reports given during the intervention procedures and in the questionnaire answers.

When CP were asked for usual actuations carried out by their physical therapists when CP experienced pain, avoiding the painful stimulus (54%), informal care (34%) and the use of analgesic medication (20%) were the most frequent strategies reported. Nevertheless, when the reporters were the physical therapists, the use of physical therapy analgesic procedures was the most frequent actuation reported (30%), followed by analgesic medication (26%), searching other professionals' advice (26%) and looking for the cause of the pain (24%). It is interesting to report that 22% of CP perceived that their physical therapist did not do enough to alleviate their pain, opinion shared by 8% of the physical therapists.

Regarding specific professional analgesic procedures, the most frequently used procedures were pharmacology, used by 62% of CP when they have pain, active exercise (used by 54% of CP), passive mobilization (56%), stretching (54%), massage (43%) and exercise in swimming-pool (43%). Three techniques were reported not having been ever used: ultrasounds, hydrotherapy and biofeedback. Percentages dropped drastically when CP were asked by the procedures that were being used in the moment of the interview: analgesic pharmacology (30%), massage (21.8%), exercise in swimming-pool (36%). The amount and duration of relief of the most effective treatments is shown in Table 3.

-Please, insert Table 3 about here-

The agreement between both groups regarding intensity and duration of relief provided by physical therapy techniques was not calculated due to the low rate of use of these procedures.

Expression and recognition of pain
Both groups (CP and physical therapists) agreed in the perception that the health professional understands the pain expression of CP. Communicative CP reported to

express pain to health professionals mainly with verbal expression (96%) and movements or changes in the body tone (18%), followed by other vocal expressions as crying and shouts (6%), facial expression (2%) and physiological sings as sweating or change of color (2%). Only 6% of persons with CP reported that they do not to express pain to the healthy professional when they felt it. When physical therapist were asked how they knew that a person with CP was suffering pain, verbal expression was again the most frequent way (40.6%), followed by other vocal expressions (26.6%), facial expression (18%), movements and changes of the body tone (17.2%) and change of social behavior (2.3%).

3.3.2 Agreement in physical therapists of communicative and non-communicative CP

Comparing the characteristics of pain reports between physical therapist of communicative and non-communicative children, no significant differences were found, apart from the non-existence of verbal pain reports and the use of more non-verbal keys to detect pain (vocal, facial, body movements and tone and CP's mood). Intensity of pain, influencing factors, interference with activities and management did not show significant differences. Nevertheless, a significant difference was found in the score of the intensity of hamstring stretching, which showed to be higher when the physical therapist reported the pain of communicative children (U Mann-Withney(48)=-2.205, p<.05).

DISCUSSION

The aim of the present study was twofold: 1) to evaluate the agreement between self-reports of pain in persons with CP and their physical therapists' reports and 2) to examine the impact of the physical therapists' intervention on CP pain. Basically, our data showed that there was a high agreement between CP self-reports and physical therapists' reports concerning the presence of chronic pain, its intensity, location and interference with daily life activities. Moreover, we found that physical therapists' reports of pain in persons with and without communicative skills were similar. It has been also observed that many common health procedures used in physical therapy were themselves sources of pain in cerebral palsy. Finally, despite the existence of well-known physical therapy analgesic techniques, physical therapists in the present study

were characterized by an elevated use of informal care in CP pain (e.g. touching, emotional support).

Our data showed high agreement between CP self-reports and physical therapists' reports concerning the presence of chronic pain, its intensity, location and interference with daily life activities. These results coincide with studies on quality of life that found also agreement between CP parents and professionals who treated CP (White-Koning et al., 2008). Similarly to other studies, there was found a high incidence of pain among persons with CP. In the present study, pain was experienced as chronic in 36% of CP participants and rated with a mean intensity of 3.5 in a 11-point VAS scale. Pain in CP was perceived by physical therapists in 31% of the cases and rated with a mean intensity of 3.4. These findings are in agreement with previous reports indicating that persons with CP often experience recurrent pain of a moderate-to-severe intensity on a daily or weekly basis that significantly interferes with daily activities (Doralp & Bartlett, 2010; Murphy KP., 2010; Parkinson et al., 2010; Malone & Vogtle, 2010; Castle et al., 2007; Gallien et al., 2007; Jahnsen et al., 2004; Hunt et al., 2003; Jensen et al., 2003; Engel et al., 2002). Our data further suggest that the pain experience reported by participants with CP was significantly above the prevalence rate of pain among the general population. In addition, the agreement showed by pain reports of children and their physical therapists indicate that physical therapists might be considered a valuable source in assessing CP pain.

Moreover, we found that physical therapists' reports of pain in persons with and without communicative skills were similar. The present study also shows that verbal expression of pain did not influence the recognition of pain by physical therapists. These results are contradictory with the results reported by Tervo et al. (2006) that reported higher pain perception in CP with communicative problems. This point is of great importance because some studies found significant positive correlations between verbal and vocal behaviors and pain intensity ratings (Hester NK., 1979) and that vocal expressions, especially crying, influence nurses' decisions to administer analgesics (Hamers et al., 1994). The use by the physical therapists of a wide arrange of non-verbal expressions of pain such as vocal, facial and body tone and movements, coincides with the results of Swiggum et al. (2010) in a study with questionnaires made to pediatric physical therapist. These findings support the idea of effectiveness of the non-verbal communication on the observation of physical signs and symptoms reported by Carelly P. (1997).

It has been also observed that many common health procedures used in physical therapy were themselves sources of pain in CP. Finally, it seems that despite the existence of well-known physical therapy analgesic techniques, physical therapists in the present study were characterized by an elevated use of informal care in the treatment of CP pain. Moreover, it has been observed that many common health procedures used in physical therapy are sources of pain in CP. These data are in line with previous literature, mostly referred to oncologic patients, showing that iatrogenic pain was rated in two thirds of children (Ljungman et al. 1999) and that most children have suffered unnecessarily from painful medical procedures as a result of insufficient knowledge about pain assessment and relief (Franck et al., 2005).

However, it is important to point out that despite this perfect knowledge of the CP pain state by physical therapists, measurement of pain intensity was largely performed unsystematically. Neither systematic behavioural observation nor pain scales were reported to be used, in the same way that findings of other authors (Swiggum et al, 2010; Lujngman et al., 1999, Dudgeon et al., 2002). Considering that the gold standard for assessing pain is self-report (McGrath P. 1987), it seems astonishing that instruments of the measurement of pain intensity, such as visual analogue scales and faces pain scales, are rarely used, in spite of the studies that assured that pain diagnostics and treatment could be improved through regular use of pain analysis and pain intensity measurement (Lujngman et al., 1999).

The effectiveness of pain interventions in persons with CP is another question that remains unanswered (Votgle LK., 2009). The number of visits to a health professional due to pain and the use of analgesic medication by the CP in our study showed to be lower than those of normal children and adolescents with back pain, limb pain, abdominal pain or headache (Roth-Isigkeit et al. 2005), but agrees with those reported by other studies with CP population (Engel et al, 2002). Despite the perception of physical therapists that physical therapy analgesic techniques are effective in the treatment of pain, our study did not show them as the preferred actuation when these professionals must deal with their patients' pain; the high use of informal care suggests that these methods are not apply in practice in such an extensive way. Carter et al., (2002) showed that first course of action for CP children's parents in front of a painful situation was giving analgesic medication, turning to health professionals and comforting their child (which involved what we have classified as informal care: touching, stroking, rocking, massaging, positioning, being with the child, managing the

child's environment and not causing additional negative stimuli). Interestingly, same strategies were found to be used by the physical therapists of our study, who would do what they could to find out the cause of pain, but might eventually call on the doctors for help in diagnosing or treating the pain. These strategies also coincide with those used by hospital nurses (Hunt et al., 2003). These findings agree with those of Broome et al. (1996) in general population, who found that non-pharmacologic techniques, such as relaxation, distraction, positioning and massage reported as used often or sometimes by over 50% of nurses and physicians of US teaching hospitals; while more specialized techniques, such as behavioural therapy, thermal modalities, transcutaneous electrical nerve stimulation (TENS) and hypnosis were reported as being administered sometimes. Our findings also agree with those of Engel et al., (2002) and Jensen et al., (2004) done in CP population, which showed low frequency of use of specialized treatments. Our study showed that specialized physical therapy techniques were not even used when painful procedures are performed, unlike in other pathologies such as cancer (Ljungman et al., 1999), and other useful informal strategies such as distraction were preferred (Miller et al, 2001). The lack of use of specialized techniques might be due to the perception of lack of effectiveness of these procedures. Engel et al. (2003), showed low rates of CP's satisfaction with general procedures used for pain relief. In addition, Jensen et al (2004) found that pain intensity did not change in 2 yrs period, although there was an increase in the frequency of use of several pain treatments in the studied subjects. However, in the same study CP's reports showed that many pain treatments were considered at least moderately helpful. In agreement to this statement, our study shows that physical therapy procedures produced in general moderate pain relief.

Nevertheless, our study has some limitations which must be taken into account in the interpretation of the results. Firstly, although our sample seems representative of the larger population, it remains small. The variable response rates were structural of the questionnaire, due to the variability of the pathology or the variability of the physiotherapy treatment that each person with CP receives, which did not allow to every CP subject to answer all the questionnaire items (ex. if a person has never experiment stretching, would leave all the items related with stretching unanswered). This led to low rate of responses in various items and it has to be considered a limitation. The use of a semistandarized interview, although adequate for this explorative purpose, has some important methodological bias, as the use of the same interview by persons with diverse cognitive and developmental abilities may cause

some distortions. In contrast to other studies, which focused on cognitively or non-cognitively impaired population separately, this study tried to address the whole CP population, with its different cognitive, communicative and functional characteristics, trying to better represent this population reality. In non-verbal CP, there remains a degree of uncertainty about the child's experience; the research is therefore limited by the inherently lack of verbal reports. Moreover, the reports were retrospective, with the known limitations that this fact may provoke.

In conclusion, it seems that physical therapists understand CP's expression of pain, even in the case of non-communicative CP, although they can base in different strategies to know it. Moreover, it seems that physical therapists do not always apply specialized pain assessment or techniques to relieve pain, despite that some of them are considered al least moderately effective. Management of pain can be improved by collaborative efforts of multidisciplinary pain teams in the institutions where CP usually attend, but standardized pain assessment and treatment for CP seems to remain an important clinical and research challenge.

REFERENCES

Anand KJ, Craig KD. New perspectives on the definition of pain. Pain. 1996;67(1):3-6.

Brattberg G. Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 2004;8:187–199.

Breau LM, McGrath PJ, Camfield C, Rosmus C, Finley GA Preliminary validation of an observational pain checklist for persons with cognitive impairments and inability to communicate verbally. Dev Med Child Neurol. 2000;42(9):609-16.

Breau LM, McGrath PJ, Camfield CS, Finley GA. Psychometric properties of the non-communicating children's pain checklist-revised. Pain. 2002;99(1-2):349-57.

Broome ME, Richtsmeier A, Maikler V, Alexander MA. Pediatric pain practices: a national survey of health professionals. J Pain Symptom Manage. 1996;11(5) 312-20.

Carelly P. Maternal knowledge and professional knowledge: co-operation and conflict in the care of sick children. Int J Nurs Stud. 1997;34(1), 27-34.

Carter B, McArthur E, Cunliffe M. Dealing with uncertainty: parental assessment of pain in their children with profound special needs. J Adv Nurs. 2002; 38(5):449-457.

Castle K, Imms C, Howie L. Being in pain: a phenomenological study of young people with cerebral palsy. Dev Med Child Neurol. 2007;49(6):445-9.

Doralp S, Bartlett DJ. The prevalence, distribution, and effect of pain among adolescents with cerebral palsy. Pediatr Phys Ther. 2010;22(1):26-33.

Dudgeon BJ, Gerrard BC, Jensen MP, Rhodes LA, Tyler EJ. Physical disability and the experience of chronic pain. Arch Phys Med Rehabil. 2002;83(2):229-35.

Engel JM, Jensen MP, Hoffman AJ, Kartin D. Pain in persons with cerebral palsy: extension and cross validation. Arch Phys Med Rehábil. 2003;84:1125–1128.

Engel JM, Kartin D, Jensen MP. Pain treatment in persons with cerebral palsy: frequency and helpfulness. Am J Phys Med Rehabil. 2002;81:291–296.

Franck LS, Allen A, Cox S, Winter I. Parents'views about infant pain in neonatal intensive care. Clin J Pain 2005; 21(2):133-9.

Gallien P, Nicolas B, Dauvergne F, Pétrilli S, Houedakor J, Roy D, Duruflé A. Pain in adults with cerebral palsy. Ann Readapt Med Phys. 2007;50(7):558-63.

Hadden KL & von Baever CL. Global and specific behavioural measures of pain in children with cerebral palsy. Clin J Pain. 2005; 21(2):140-6.

Hadden KL, Von Baeyer CL. Pain in children with cerebral palsy: common triggers and expressive behaviors. Pain. 2002;99(1-2):281-288.

Hamers JP, Abu-Saad HH, Halfens RJ, Schumacher JN. Factors influencing nurses' pain assessment and interventions in children. J Adv Nurs. 1994;20(5):853-60.

Hester NK. The preoperational child's reaction to immunization. Nurs Res. 1979;28(4):250-5.

Hilberink SR, Roebroeck ME, Nieuwstraten W, Jalink L, Verheijden JM, Stam HJ. Health issues in young adults with cerebral palsy: towards a life-span perspective. J Rehabil Med. 2007;39(8):605-11.

Hunt A, Mastroyannopoulou K, Goldman A, Seers K. Not knowing- the problem of pain in children with severe neurological impairment. Int J Nurs Stud. 2003; 40:171-183.

Jahnsen R, Villien L, Aamodt G, Stanghelle JK, Holm I. Musculoskeletal pain in adults with cerebral palsy compared with the general population. J Rehabil Med. 2004;36(2):78-84.

Jensen MP, Engel JM, Hoffman AJ, Schwartz L. Natural history of chronic pain and pain treatment in adults with cerebral palsy. Am J Phys Med Rehabil, 2004; 83(6):439-45.

Jensen MP, Engel JM, McKearnan KA, Hoffman AJ. Validity of pain intensity assessment in persons with cerebral palsy: a comparison of six scales. J Pain. 2003;4(2):5.

Jóźwiak M, Harasymczuk P, Koch A, Kotwicki T. Incidence and risk factors of hip joint pain in children with severe cerebral palsy. Disabil Rehabil. 2011;33(15-16):1367-72.

Kibele A. Occupational therapy's role in improving the quality of life for persons with cerebral palsy. Am J Occup Ther. 1989;43:371-317.

Lannin NA, Novak I, Cusick A. A systematic review of upper extremity casting for children and adults with central nervous system motor disorders. Clin Rehabil. 2007;21(11):963-76.

Ljungman G, Gordh T, Sörensen S, Kreuger A. Pain in paediatric oncology: interviews with children, adolescents and their parents. Acta paediatr. 1999;88: 623-30.

Malone LA, Vogtle LK. Pain and fatigue consistency in adults with cerebral palsy. Disabil Rehabil. 2010;32(5):385-91.

McGrath PA. An assessment of children's pain: a review of behavioral, physiological and direct scaling techniques. Pain. 1987;31(2):147-76.

McGrath PJ, Rosmus C, Canfield C, Campbell MA, Hennigar A. Behaviours caregivers use to determine pain in non-verbal, cognitively impaired individuals. Dev Med Child Neurol. 1998;40(5):340-3.

McKearnan KA, Kieckhefer GM, Engel JM, Jensen MP, Labyak S. Pain in children with cerebral palsy: a review. J Neurosci Nurs. 2004;36:252-259.

Miller C, Johan-Murphy M. Impact of the therapist-child dyad on children's pain and coping during medical procedures. Dev Med Child Neur. 2001, 43:118-123.

Murphy KP. The adult with cerebral palsy. Orthop Clin North Am. 2010;41(4):595-605.

Nolan J, Chalkiadis GA, Low J, Olesch CA, Brown TC. Anaesthesia and pain management in cerebral palsy. Anaesthesia. 2000;55(1):32-41.

Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care 2003; 41: 582–92.

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39(4): 214-23.

Parkinson KN, Gibson L, Dickinson HO, Colver AF. Pain in children with cerebral palsy: a cross-sectional multicentre European study. Acta Paediatr. 2010;99(3):446-51.

Roth-Isigkeit A, Thven U, Stöven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: restrictions in daily living and triggering factors. Pediatrics, 2005; 115(2):52-62.

Russo RN, Miller MD, Haan E, Cameron ID, Crotty M. Pain characteristics and their association with quality of life and self-concept in children with hemiplegic cerebral palsy identified from a population register. Clin J Pain. 2008;24(4):335-42.

Schwartz L, Engel JM, Jensen MP. Pain in persons with cerebral palsy. Arch Phys Med Rehabil. 1999;80:1243-1246.

Swiggum M, Hamilton ML, Gleeson P, Roddey T, Mitchell K. Pain assessment and management in children with neurologic impairment: a survey of pediatric physical therapists. Pediatr Phys Ther. 2010;22(3):330-5.

Tervo RC, Symons F, Stout J, Novacheck T. Parental report of pain and associated limitations in ambulatory children with cerebral palsy. Arch Phys Med Rehabil. 2006;87(7):928-934.

Vargus-Adams JN, Martin LK. Domains of importance for parents, medical professionals and youth with cerebral palsy considering treatment outcomes. Child Care Health Dev. 2011;37(2):276-81.

Varni JW, Burwinkle TM, Seid M. The PedsQL as a pediatric patient-reported outcome: reliability and validity of the PedsQL Measurement Model in 25,000 children. Expert Rev Pharmacoecon Outcomes Res. 2005;5(6):705-19.

Vogtle LK. Pain in adults with cerebral palsy: impact and solutions. Dev Med Child Neurol. 2009;51 Suppl 4:113-21.

White-Koning M, Arnaud C, Dickinson HO, Thyen U, Beckung E, Fauconnier J, McManus V, Michelsen SI, Parkes J, Parkinson K, Schirripa G, Colver A. Determinants of child-parent agreement in quality-of-life reports: a European study of children with cerebral palsy. Pediatrics. 2007;120(4):e804-14.

White-Koning M, Grandjean H, Colver A, Arnaud C. Parent and professional reports of the quality of life of children with cerebral palsy and associated intellectual impairment. Dev Med Child Neurol. 2008;50(8):618-24.

TABLE AND GRAPHIC LEGENDS

Table 1. Clinical characteristics of persons with cerebral palsy (n=128) shown in two groups, according to their capacity of communication. Number of persons classified according with sex, type of cerebral palsy, cognitive and motor impairment (following the Gross Motor Function Classification Scale).

Table 2. Mean, standard deviation and coefficient of agreement on intensity of pain produced by painful health procedures according to CP and physical therapists perception. Intensity of pain was measured by a 11-point scale, being 0=No pain and 10=The maximum pain possible.

Table 3. Mean and standard deviation of intensity and duration of relief produced by the most effective physical therapy procedures according to CP and physical therapists perception. Intensity of relief was measured by a 11-point scale, being 0=No pain and 10=The maximum pain possible. Duration of relief was classified with the following scale: 0=No relief, 1=Less than 1 hour, 2=1-3 hours, 3=3-6 hours, 4=6-12 hours, 5=12-24 hours, 6=24-48 hours, 7=More than 48 hours.

Table 1.

Clinical variable	Communicative cerebral palsy (n=50)	Non-communicative cerebral palsy (n=78)
Sex	21 females	24 females
Age	16.88 (13.93)	19.31 (10.43)
Type of cerebral palsy		
Bilateral spastic	35	50
Unilateral spastic	7	3
Diskinetic	4	13
Ataxic	4	7
Mixed	0	5
Motor impairment (GMFCS)		
Level 1	13	5
Level 2	17	5
Level 3	7	12
Level 4	10	11
Level 5	3	45
Cognitive impairment		
None	35	12
Mild	7	8
Moderate	8	12
Severe	0	46

Table 2.

Sanitary procedure	Pain intensity		Coeficient of agreement
	CP (n=50)	Physical therapists (n=18)	
Chirurgic intervention	5.43 (4.49)	4.82 (3.51)	-
Stretching	4.31 (3.45)	3.73 (3.08)	.008
Botulim toxin injection	3.77 (3.90)	4.24 (2.98)	-
Assistive standing	2.59 (3.78)	2.10 (2.63)	.009
Splints	2.38 (3.38)	2.60 (2.81)	-
Assistive walking	2.08 (3.33)	2.00 (2.45)	.025
Passivejoint mobilization	1.50 (2.37)	1.59 (2.64)	.004
Clinical assessment	0.87 (1.57)	0.94 (1.86)	.006
Assistive sitting	0.73 (2.27)	1.22 (2.29)	.001
Cleaning procedures	0.37 (1.45)	1.22 (2.69)	.027
Massage	0.18 (0.73)	1.06 (2.01)	-

- No agreement calculated because of response rates lower than 50%.

Table 3.

Analgesic treatment	Intensity of relief		Duration of relief	
	CP (n=50)	PT (n=18)	CP (n=50)	PT (n=18)
Massage	7.35 (3.17)	6.03 (2.40)	2.40 (2.00)	3.24 (1.43)
Pharmacological treatment	6.71 (3.73)	7.31 (2.21)	2.28 (1.16)	5.20 (1.03)
Exercises in the swimming-pool	6.30 (3.81)	7.36 (2,57)	3.28 (1.81)	4.35 (1.23)
Relaxation	6.05 (4.31)	5.89 (2.29)	2.36 (1.55)	3.04 (1.40)
Criotherapy	5.90 (3.63)	6.17 (0.41)	1.50 (0.53)	4.40 (1.82)
Thermotherapy	5.58 (3.85)	6.22 (2.54)	2.11 (1.27)	3.71 (1.98)

Experimento 2. Procesamiento de las aferencias somatosensoriales en las personas con parálisis cerebral.

Presentación de la investigación

La primera fase de la investigación confirmó la existencia de una percepción dolorosa aumentada y una percepción de la sensación táctil disminuída en personas con parálisis cerebral. La segunda fase se dedicó a la profundización experimental en el procesamiento somatosensorial del dolor y la sensibilidad táctil de esta población, comparándola con el de la población sana.

Debido a que en nuestra primera fase de la investigación la experiencia somatosensorial se relacionó con la edad en la población control sana, pero no en la población con parálisis cerebral, se persistió en un diseño de estudio por edades. De este modo, en un primer experimento se compararon medidas periféricas de sensibilidad propioceptiva, táctil y dolorosa, así como los correlatos cerebrales del procesamiento somatosensorial, de niños sanos, adultos sanos, niños con parálisis cerebral y adultos con parálisis cerebral.
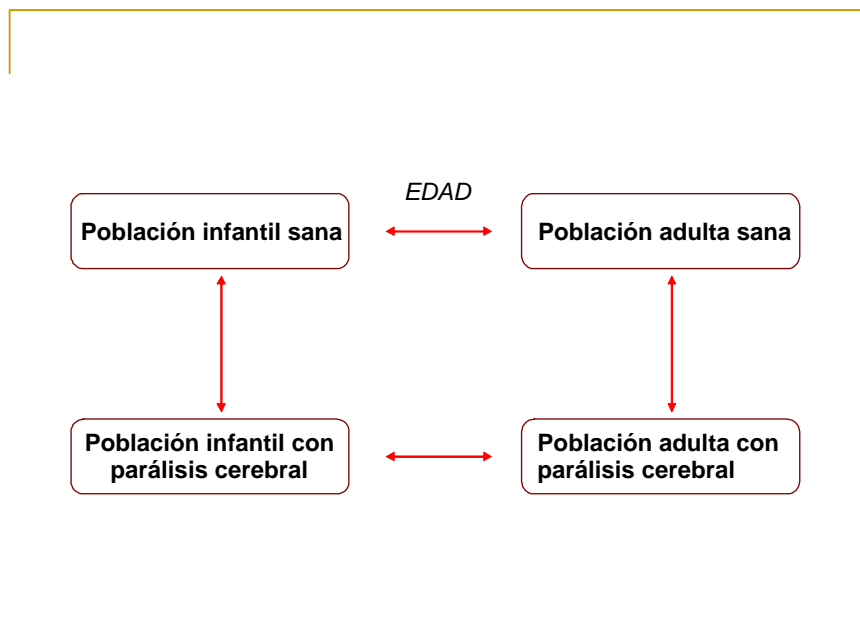
De esta forma, la exploración de los diferentes mecanismos que podrían influir en el mantenimiento de los déficits somatosensoriales a lo largo del tiempo en las personas

con parálisis cerebral se realizó con un diseño experimental donde se combinó el análisis de medidas periféricas de propiocepción, dolor y sensibilidad táctil con el análisis de la actividad cerebral provocada por estimulación táctil no dolorosa. El propósito de esta experimentación era comprobar, con medidas instrumentales, la existencia de dolor y déficits de la sensibilidad táctil y propioceptiva que, corroborando la literatura, habían sido expresados en los cuestionarios de la fase anterior por personas con parálisis cerebral. Además, y dado que la afectación neurológica provocada por la patología debía afectar también al procesamiento de las aferencias sensitivas, otro de nuestros objetivos era explorar el procesamiento de aferencias sensitivas no dolorosas por la corteza somatosensorial. Para ello utilizamos un análisis de la señal electroencefalográfica sobre la corteza parietal, más concretamente, de los potenciales evocados somatosensoriales (SEP), procedimiento comunmente utilizado en el análisis de la actividad eléctrica cerebral, pero que había sido poco empleado en el estudio de la afectación somatosensorial de personas con parálisis cerebral. Las conclusiones de esta primera fase de la investigación, se publicaron con el título de *Developmental changes in somatosensory processing in cerebral palsy and healthy individuals* en la revista Clinical Neurophysiology, en 2010.

Debido a que algunos estudios refieren un desplazamiento de las áreas cerebrales somatosensoriales dependientes de la lesión neurológica o de la calidad de las aferencias periféricas recibidas (Eyre, 2007; Gerloff et al., 2006; Flor, 2003), de forma previa a analizar el procesamiento somatosensorial descrito anteriormente debíamos comprobar que el procesamiento de la información táctil de las personas con parálisis cerebral se realizaba en la localización parietal de la corteza cerebral. Para ello se realizó un estudio de **localización de fuentes** de la actividad eléctrica de la corteza cerebral ante un estímulo táctil con el programa S-Loreta, cuyos datos no se publicaron. Este estudio se realizó siguiendo el diseño descrito anteriormente donde se comparaban los parámetros GRUPO (sanos vs. parálisis cerebral) y EDAD (niños vs. adultos). En él participaron 15 niños sanos (9 mujeres, edad entre 5 y 14 años), 15 adultos sanos (1 mujer, edad entre 22 y 42 años), 15 niños con parálisis cerebral (7 mujeres, edad entre 5 y 14 años) y 14 adultos con parálisis cerebral (3 mujeres, edad entre 22 y 55 años). La estimulación táctil se realizó de forma bilateral en labios y pulgares con un estimulador neumático, consistente en una membrana adherida a la superficie cutánea que se hincha y deshincha en cada estímulo. Los estímulos se realizaron en bloques de 120 estímulos de 100 ms.

de duración, con una presión de 2 bares y un intervalo interestímulo variable de 1000 +/- 50 ms. La actividad eléctrica cerebral se registró durante la estimulación con un amplificador de EEG de 64 canales en los participantes adultos y de 20 canales en los niños, con una tasa de muestreo de 1000 Hz. y filtros 0.1-40 Hz. Una señal digital desde el estimulador neumático actuó como trigger para el registro de SEP. Para el análisis de localización de fuentes se utilizaron 19 canales (Fp1 Fp2 F7 F3 Fz F4 F8 T3 C3 Cz C4 T4 T5 P3 Pz P4 T6 01 02), en ventanas temporales 700 ms. El análisis se centró en la localización de las señales postestímulo tempranas (P50, P100), dado que previos estudios realizados por el grupo de investigación habían demostrado que los estímulos sensoriales no dolorosos provocaban SEP identificables en varias latencias entre los 50 y 125 ms. (Montoya et al., 2006; Montoya & Sitges, 2006). Para el análisis estadístico de los datos se utilizo una Log ratio de las medias y una aleatorizacion de 5000 permutaciones para un analisis no parametrico, que permitía poder corregir el umbral critico y el valor de p. Este estudio confirmó que las personas con parálisis cerebral percibían los estímulos táctiles en el área S1, en la corteza somestésica, lo que sentó las bases para un correcto análisis de las señales eléctricas cerebrales de los experimentos posteriores. A continuación, pueden contemplarse los gráficos que demuestran los resultados de esta fase previa.
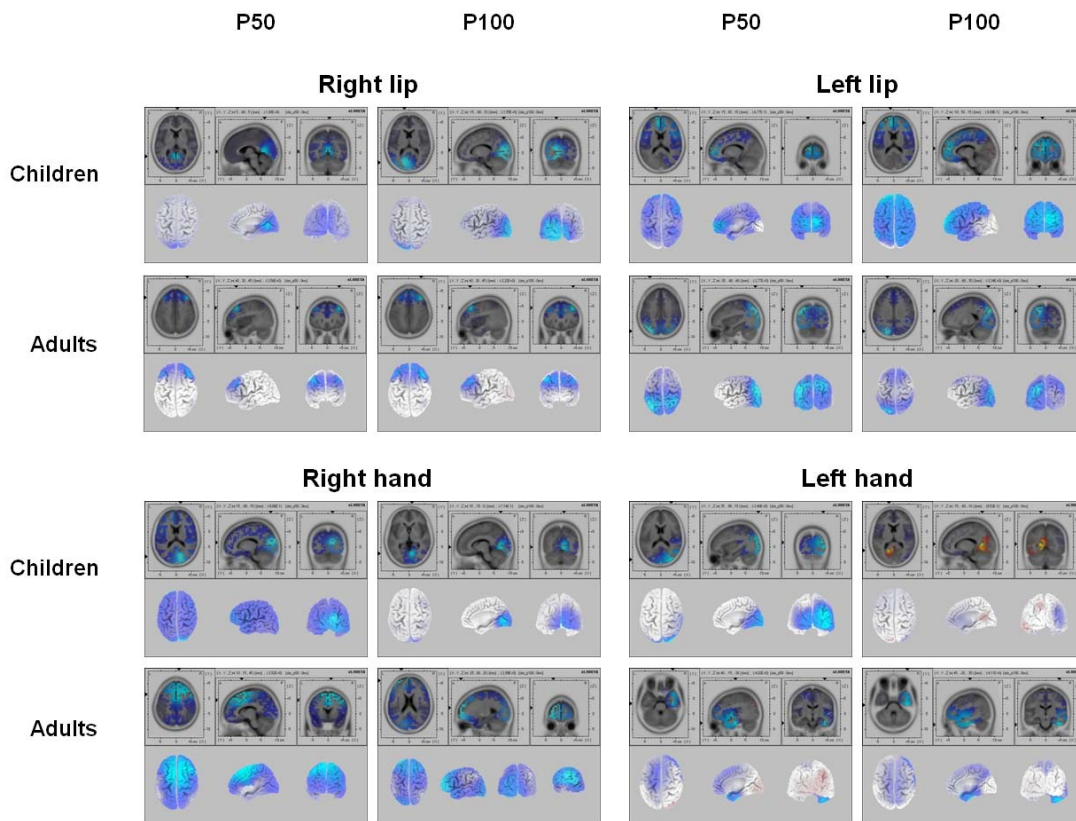
Figura 5. Imágenes de localización de fuentes de un estímulo táctil no doloroso en labios y manos de niños y adultos con parálisis cerebral.

Las fuentes de actividad eléctrica cerebral se localizaron en el lóbulo parietal, áreas 17 y 19 de Brodman y precuneus para la estimulación táctil de los labios y en el lóbulo parietal, área 10 y 18 de Brodman y cuneous o giro frontal superior para la estimulación táctil de las manos. Finalmente, el análisis de la localización de fuentes mediante sLORETA reveló diferencias significativas entre los sujetos con parálisis cerebral y los voluntarios sanos sobre diferentes regiones del lóbulo parietal. La activación resultó menor para adultos control que para adultos con PC en P50 y P100 en el labio izquierdo y en P50 de la mano derecha (ps<.05). Lo mismo sucedió con la población infantil en P100 del labio derecho y P50 de la mano izquierda (ps<.05). Los sujetos control, presentaron diferencias debidas a la edad en varias zonas corporales (P50 en labio derecho, P50 y P100 en labio izquierdo, P50 y P100 en mano derecha y P100 en mano izquierda), mostrando que los niños presentaban mayor activación que los adultos. Estas diferencias sólo se vieron en P50 en labio izquierdo en la población con parálisis cerebral, donde los niños también presentaron mayor activación que los adultos. Estos resultados confirmaron dos premisas importantes para nuestro estudio: 1) la sensibilidad

táctil está localizada en el lóbulo parietal también en las personas con parálisis cerebral y 2) la edad es un importante factor a explorar y debía mantenerse en el diseño del estudio.

Debido a que el primer estudio de esta fase arrojó como resultado la presencia de una asimetría en el procesamiento somatosensorial de las personas con parálisis cerebral al estimular hemicuerpos distintos, asimetría que no aparecía en las personas sanas, se decidió analizar de nuevo los datos de los sujetos con parálisis cerebral que habían tomado parte en el estudio anterior. Se escogió a los sujetos que presentaban exclusivamente una afectación motora bilateral (sujetos muy poco estudiados en la literatura), y se los dividió en dos grupos, según el lado del cuerpo en el que predominara su afectación motriz: sujetos con predominio de afectación motriz en el hemicuerpo derecho y sujetos con predominio de afectación motriz en hemicuerpo izquierdo. El objetivo de este estudio era comprobar si la asimetría entre hemisferios detectada en el procesamiento somatosensorial en el estudio anterior, se relacionaba de algún modo con la asimetría en la afectación motriz que es habitual en esta patología. Los resultados de estos análisis pueden revisarse a continuación en el manuscrito *Differences in the somatosensory processing due to the dominant hemispheric motor impairment in cerebral palsy.*

Además, y dado que existe evidencia en la literatura de que la espasticidad puede ser un factor determinante en la existencia de déficits sensitivos (Lesny et al., 1993) y en los parámetros de los SEP (Frascarelli et al., 2011; Boćkowski et al., 2007; Park et al., 2002), se analizó si la **presencia de espasticidad** podría ser la causa de las diferencias observadas en la percepción somatosensorial. Así, dividimos nuevamente a nuestra muestra según si presentaban una parálisis cerebral espástica (n=20; media de edad=19.15, SD=14.11) o no espástica (n=8; media de edad=21.38, SD=11.49), comparándolos con el grupo control de voluntarios sanos de la misma edad (n=20; media de edad=18.55, SD=11.96). No se encontraron diferencias significativas ni en los umbrales de sensibilidad táctil, ni en los umbrales de sensibilidad dolorosa, ni en los SEP, en P50. En P100, se encontraron diferencias significativas en las amplitudes de los SEP sobre C4 en la mano izquierda (F(2,47)=3.64, p<.05). Estos resultados señalan que las diferencias producidas con respecto a los controles sanos, son debidas principalmente al grupo de no espásticos, que presentó amplitudes de los SEP significativamente mayores que el grupo control y el grupo de espásticos (ps<.05). Así,

podemos concluir que los déficits en el procesamiento somatosensorial de las personas con parálisis cerebral, estarían más relacionadas con la edad que con la presencia de de espasticidad o el tipo clínico de parálisis cerebral. Estos resultados contrastarían con los de Lesny et al. (1993) que observaron que los déficits sensitivos se presentaban de forma más marcada en el tipo espástico y menos marcada en el tipo atetoide, por lo que sería necesario realizar nuevos estudios, con un diseño que equiparara las muestras y centrado en rangos concretos de edad, para poder obtener conclusiones definitivas.

Esta fase de la experimentación confirmó la presencia de déficits somatosensoriales en las personas con parálisis cerebral, que presentaron una sensibilidad dolorosa aumentada y una sensibilidad táctil reducida con respecto a los controles sanos de su misma edad. Además, el procesamiento de las aferencias somatosensoriales también se encontró alterado en las personas con parálisis cerebral, que presentaron amplitudes de los SEP tempranos (P50, P100) mayores que los controles sanos. Se manifestó además una asimetría hemisférica en el procesamiento somatosensorial dependiendo del hemicuerpo más afectado por la lesión motora, lo que sugeriría una diferente reorganización somatosensorial tras la lesión dependiendo del predominio hemisférico de la lesión motora y nos permitió relacionar por primera vez los déficits motores y somatosensoriales en las personas con parálisis cerebral.

Manuscrito:

Developmental changes in somatosensory processing in cerebral palsy and healthy individuals

Developmental changes in somatosensory processing in cerebral palsy and healthy individuals

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ABSTRACT

Objective: Cerebral palsy (CP) is a motor disorder that causes physical disability in human development. Recent work has shown that somatosensory deficits are a serious problem for people with CP. There is however no information about the influence of age on brain correlates of tactile sensitivity.
Methods: Proprioception, touch and pain pressure thresholds, as well as somatosensory evoked potentials (SEP) elicited by tactile stimulation in lips and thumbs were examined in 15 children with CP (range 5–14 y), 14 adults with CP (range 22–55 y), 15 healthy children (range 5–14 y), and 15 healthy adults (range 22–42 y).
Results: Children with CP as compared to healthy controls showed more reduced sensitivity for non-painful stimuli, but enhanced sensitivity for painful stimuli. Early SEP amplitudes (P50 and P100) were more enhanced in children and adults with CP than in healthy participants. A functional hemispheric asymmetry was observed in CP when left- and right-side body parts were stimulated.
Conclusions: Data suggest the possibility that altered somatosensory brain processing in CP might be reflecting an enhanced excitability of the somatosensory cortex.
Significance: Assessment of somatosensory functions may have implications for future neuromodulatory treatment of pain complaints and motor rehabilitation programs in children and adults with cerebral palsy.

1. Introduction

Although classically cerebral palsy (CP) has been described mainly as a motor disability disorder, it is also known that this pathology usually is associated with disorders such as epileptic seizures, growth disorders, cognitive deficits and sensory alterations, including abnormal perception of touch and altered pain sensitivity. In this sense, it has been shown that children with CP have poorer tactile discrimination, stereognosis and proprioception compared with healthy children (Cooper et al., 1995; Sanger and Kukke, 2007; Wingert et al., 2009). Although the physiological mechanisms are still unknown, it has been proposed that somatosensory deficits could be due to primary injuries in cortical and subcortical somatosensory areas, as well as to secondary effects provoked by motor limitations which reduce child's opportunities to explore and provide an aberrant feedback of the motor movements (Clayton et al., 2003). Recent neuroimaging studies have provided evidence of significant alterations in white matter fibers connecting to sensory cortex (radiata and internal capsule), suggesting that CP injuries might be reflecting disruption of sensory as well as motor connections (Hoon et al., 2002; Thomas et al., 2005; Hoon et al., 2009). Moreover, it has been suggested that the monotonous and stereotypical patterns of spontaneous movements in children with hemiplegic cerebral palsy could result in abnormal sensory feedback and altered cortical reorganization, thus leading to somatosensory processing deficits (Coq et al., 2008).

Development is generally associated with an improvement of sensory functions, due to the maturation of the neural pathways. It is also increasingly evident that the developing nervous system is dependent upon postnatal neural activity, requiring defined patterns of afferent input for normal synaptic organization to take place. Abnormal activity related to pain and injury in early life may therefore have the potential to cause long-term changes in somatosensory and pain processing (Schmelzle-Lubiecki et al., 2007). Although there is evidence suggesting that injuries occurring at early ages are usually associated with a more extensive reorganization and better functional outcome in individuals with cerebral palsy (Coq et al., 2008), little is known about age-related changes in somatosensory processing, including pain associated with cerebral palsy. In the present study, we measured somatosen-

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sory processing at different functional levels with psychophysical and brain recording techniques. In particular, our research was mainly addressed to evaluate differences in touch and pain pressure sensitivity, as well as in somatosensory brain activity elicited by non-painful tactile stimulation among healthy volunteers and persons with CP, taking into account possible age-related differences in these sensitivity measures.

2. Methods

2.1. Participants

Subjects with cerebral palsy (CP) and healthy subjects were recruited from educational and occupational centers established in the island of Majorca (Spain) between July and September 2008. A group of 250 potential subjects were initially identified by their own physicians and invited to participate using an informational letter explaining the details of the research study. Inclusion criteria were: (1) age between 5 and 14 years old and older than 20, and (2) cognitive level that allows understanding the instructions. Augmentative communication devices and information from parents and caregivers were used as needed to facilitate data collection in subjects with communication difficulties.

Fifteen children with CP (7 females, 8 males; mean age 9 y 1mo, SD 3 y 7mo, range 5–14 y), 14 adults with CP (3 females, 11 males; mean age 33 y 8mo, SD 10 y 4mo, range 22–55 y), 15 healthy children (9 females, 6 males; mean age 9 y 11mo, SD 3 y 8mo, range 5–14 y), and 15 adults (1 female, 14 males; mean age 28 y 11 mo, SD 7 y 4mo, range 22–42 y) decided to participate in the study. Subjects or their parents reported their age, sex, medication and treatment history. The type of cerebral palsy, prematurity, cognitive level and location of cerebral impairment were obtained from the health history, and the level of motor impairment was determined using the Gross Motor Function Classification Scale (GMFCS) (Palisano et al., 1997). Table 1 displays clinical characteristics of participants with cerebral palsy within each age group.

All participants granted written informed consent according with the Declaration of Helsinki. In the case of children, parents or juridical tutors gave their informed consent. The study was approved by the Ethics Committee of the Regional Government of the Balearic Islands.

2.2. Somatosensory testing

All participants in the study were administered following tasks to measure somatosensory processing and sensitivity:

2.2.1. Proprioceptive task

To assess proprioceptive skills, two different tasks were performed with eyes-closed and in all joints of the upper limb: (a) recognition of the existence of movement, and (b) final position in passive movement of a joint reported verbally or performance of the same movement with the contralateral limb. Each task was repeated five times and the average number of correct trials was used as an index of proprioceptive skills. This procedure has been used successfully in previous studies (Wingert et al., 2008).

2.1.2. Touch

Touch sensitivity using von Frey monofilaments (Keizer et al., 2008) was measured bilaterally at two body locations (lips and thumb finger). Von Frey monofilaments were composed by a set of plastic filaments of different diameter (0.14–1.01 mm.). The test was performed touching the skin in a perpendicular way, pressing it slowly down until it buckles, holding it steady during 1.5 s and removing it in the same way as it was applied. After several trials to assure the understanding of the procedure, subjects were instructed to notify the experimenter if they felt any sensation of touch by saying "yes" or "no". The procedure started with a thick filament and depending on subjects' answers, thicker or thinner filaments were applied. The sensitivity score for each body location was calculated as the mean of the three thinnest filaments detected. Null stimuli were also used to find false positive responses

Table 1
Clinical characteristics of individuals with cerebral palsy. (M = male, F = female, BS = bilateral spastic, US = unilateral spastic, D = dyskinetic, A = ataxic, R = right and L = left).

ID	Sex	Age	CP subgroup	Gestational age (weeks)	GMFCS	Mental retardation	Epilepsia	Medication
1	F	5	BS	27	5	Severe	No	No
2	M	5	BS	40	1	No	No	No
3	F	6	BS	31	5	No	No	No
4	F	7	BS	20	4	Mild	Yes	Antiepileptic
5	M	7	BS	24	1	No	No	Muscular relaxant
6	M	7	A	40	2	Moderate	Yes	No
7	M	7	A	28	1	No	Yes	Antiepileptic
8	F	7	BS	40	3	No	Yes	Antiepileptic
9	M	9	BS	40	2	Moderate	Yes	Antiepileptic
10	M	9	BS	41	3	No	No	No
11	F	11	BS	28	2	No	No	No
12	F	12	BS	36	2	No	Yes	Antiepileptic
13	F	12	A	40	4	No	No	No
14	M	12	US	32	2	No	No	No
15	M	12	BS	31	3	Mild	No	Antidepressive
16	M	21	A	40	1	Moderate	No	No
17	M	26	BS	40	1	Moderate	No	No
18	M	27	BS	40	1	Moderate	No	No
19	M	27	D	40	4	No	Yes	Antiepileptic
20	M	27	BS	40	3	Moderate	No	No
21	M	28	BS	40	1	Severe	No	Antidepressive
22	M	28	A	40	2	Severe	Yes	No
23	M	30	BS	30	3	No	Yes	No
24	F	30	D	42	5	No	Yes	Antidepressive
25	F	35	BS	40	2	Severe	Yes	Antiepileptic
26	M	38	A	40	2	Mild	Yes	Antiepileptic
27	M	46	US	40	2	Moderate	Yes	Antiepileptic
28	F	52	BS	40	4	No	Yes	Antiepileptic
29	M	54	D	32	1	Mild	NO	Muscular relaxant

and responses delayed more than 3 s were noted as abnormal. Body locations were stimulated in a pseudo-randomized order.

2.1.3. Pressure pain

Pressure pain thresholds (expressed in kgf/cm^2) were measured with a digital dynamometer and using a flat rubber tip (1 cm^2). Subjects were asked to say 'pain' when the pressure became painful. Pressure was released when either the pain detection threshold had been reached or when the maximum pressure of the algometer (equal to 13.0 kgf) was reached. Pressure stimuli were applied bilaterally in pseudo-randomized order at the same two body locations as before (lips and thumb finger). Before the assessment, subjects were familiarized with the procedure using non-painful ranges to relieve potential anxiety. The reliability of this procedure for assessing pressure pain sensitivity has been demonstrated in previous studies (Cathcart and Pritchard, 2006).

2.3. Brain activity elicited by touch

Somatosensory evoked potentials (SEP) elicited by tactile stimuli were recorded in a sound attenuated, semi-darkened room. Subjects were seated in a reclining chair and encouraged to relax and to keep their eyes closed. In younger children, mother was allowed to remain in the room if the child was anxious. Non-painful tactile computer-controlled impulses were delivered at the same body locations as before using a pneumatic stimulator, consisting of a small membrane attached to the body surface by a plastic clip and fixated with adhesive strips. Each stimulation block consisted of 120 stimuli of 100 ms duration with an approximate pressure of 2 bars and a variable inter-stimulus interval of 1000 ± 50 ms. This type of tactile stimulation has been already used in previous research of our lab to study somatosensory processing in healthy (Montoya and Sitges, 2006) and chronic pain patients (Montoya et al., 2006). Electrical brain activity was registered during the stimulation with a 64-channel EEG amplifier in adults and with a 20-channels EEG amplifier in children. Electrodes were placed following the international 10/20 system and referenced to Cz. Vertical electrooculograms (EOG) were recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 10 kOhm. The sampling rate was 1000 Hz. Filter bandpass was set at 0.1–40 Hz. A digital signal from the tactile stimulation device was used as a trigger for SEP acquisition. SEPs were averaged relative to a 150-ms prestimulus baseline.

Our previous work has shown that this kind of non-painful tactile stimulus evoke a typical SEP with readily identifiable components at several latencies between 50 and 125 ms (Montoya et al., 2006; Montoya and Sitges, 2006). According with these studies and based on visual inspection of the average waveforms, we calculated mean SEP amplitudes in the following two time windows for each channel and body location: 20–70 ms (P50) and 70–120 ms (P100) after stimulus onset.

2.4. Statistical analysis

To assess the statistical effects on sensitivity measures, multivariate analyses of variance for repeated measures with between-subject factors PATIENT GROUP (CP vs. healthy) and AGE GROUP (children vs. adults), as well as within-subject factors BODY LOCATION (thumb vs. lip) and STIMULATION SIDE (left vs. right) were computed. SEP amplitudes over central and parietal electrodes (C3, C4, P3, P4) were analyzed by using multivariate analyses of variance for repeated measures with the additional within-subject factors BRAIN HEMISPHERE (contralateral vs. ipsilateral to stimulated body side). In all cases, interaction effects were assessed using post-hoc pairwise comparison tests provided by the MANOVA procedure in the SPSS package.

3. Results

3.1. Somatosensory testing

Proprioceptive skills were unaffected in all healthy participants. The percentage of correct trials in both tasks was of 100% in healthy individuals, yielding an average score of 5 out of 5. By contrast, proprioceptive skills in cerebral palsy were altered in cerebral palsy. Proprioception scores were significantly reduced in both children (mean score = 4.33, SD = .76) and adults with cerebral palsy (mean score = 3.67, SD = 1.97) as compared with healthy children (Chi-square [3] = 11.84, $P < .01$) and adults (Chi-square [3] = 8.75, $P < .05$), respectively. No significant group differences were found between CP children and CP adults.

Fig. 1 displays the mean touch sensitivity in lip and thumb for each group (cerebral palsy vs. healthy controls) and age group (children vs. adults), separated by body locations (right vs. left). The lip was significantly more sensitive than the thumb for touch stimulation in all participants (main effect of BODY LOCATION: $F(1,55) = 58.61$, $P < .0001$). In addition, a significant interaction of BODY LOCATION × PATIENT GROUP × AGE GROUP was found ($F(1,55) = 6.54$, $P < .05$). Post-hoc pairwise comparisons of this interaction effect indicated that the lip was more sensitive than the thumb in children with CP ($P < .001$), healthy children ($P < .001$), and healthy adults ($P < .001$), but not in adults with CP. Post-hoc comparisons also revealed that children with CP had more reduced touch sensitivity than healthy children in the lips ($P < .05$) and marginally in the thumbs ($P < .1$), whereas no significant differences between CP and healthy were observed in adults. Neither CP nor healthy participants showed differences between children and adults.

Pressure pain sensitivity was also higher at the lip than at the thumb for all participants (main effect of BODY LOCATION: $F(1,55) = 276.04$, $P < .0001$). Moreover, a significant interaction effect of STIMULATION SIDE × PATIENT GROUP ($F(1,55) = 4.17$, $P < .05$) was found, indicating that CP participants were more sensitive to pain than healthy controls on the left-side of the body ($P < .05$), and that CP participants were more sensitive on the left than on the right-side of the body ($P < .05$). In order to further clarify group and age-related differences in pain sensitivity, a further analysis was conducted separately for each body location. A significant interaction effect of PATIENT GROUP × AGE GROUP was found for pressure pain sensitivity on the lip ($F(1,55) = 6.78$, $P < .05$), showing that pain sensitivity in this area was more enhanced in children with CP than in healthy children ($P < .05$), but not in adults. Moreover, post-hoc pairwise comparisons revealed that children with CP had more increased pain sensitivity than adults on thumb ($P < .001$) and lip ($P < .05$), whereas healthy children were more sensitive than adults for painful stimulation on the thumb ($P < .01$), but not on the lip.

3.2. Brain activity elicited by non-painful body stimulation

Somatosensory evoked potentials (SEPs) elicited by the stimulation of lip and thumb over the contralateral hemisphere are shown in Fig. 2. Within the first 150-ms interval, SEPs were characterized by a prominent positive peak around 50 ms (P50), followed by a second positive peak around 100 ms after stimulus onset (P100). These peaks were clearly observable after thumb stimulation in healthy controls. Due to difficulties associated with peak detection after visual inspection of individual averages, mean amplitudes in two time windows were computed and statistically analyzed.
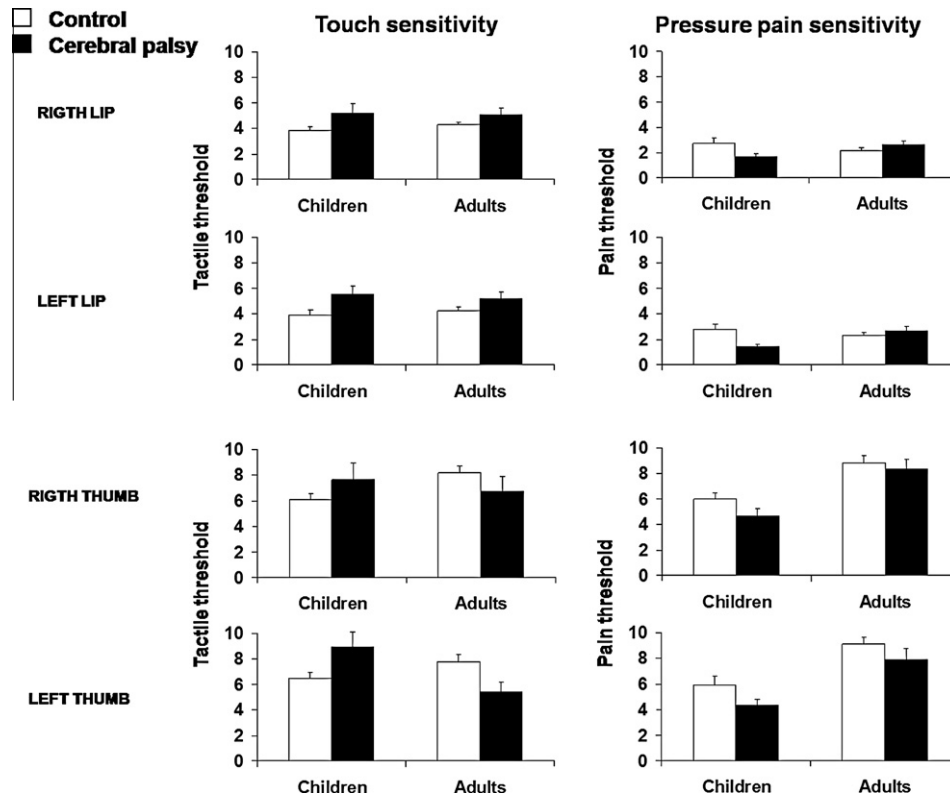
Fig. 1. Means of touch and tactile sensitivity scores in healthy and in cerebral palsy participants separated by age group.

Fig. 2. Grand averages of somatosensory evoked potentials elicited by tactile stimulation of lips and thumbs in cerebral palsy and healthy controls, separated by age group. The time-windows used for computing mean P50 and P100 amplitudes are marked by a rectangle.

3.2.1. Mean P50 amplitude

Statistical analyses of brain activity confirmed that P50 amplitudes were significantly higher over the contralateral hemisphere than over the ipsilateral hemisphere to the stimulation side (main effect of BRAIN HEMISPHERE: $F(1,55) = 26.52$, $P < .001$). There was also a significant AGE × PATIENT GROUP interaction effect ($F(1,55) = 4.96$, $P < 0.5$), showing that age differences appeared in healthy participants, but not in individuals with CP. Post-hoc pairwise comparisons revealed that P50 amplitudes were higher in healthy children than in children with CP children ($P < .05$), and

healthy adults ($P < .05$). No significant differences on P50 amplitudes were found between healthy and CP adults. In addition, a significant four-way interaction of BRAIN HEMISPHERE × BODY LOCATION × AGE × PATIENT GROUP ($F(1,55) = 4.62$, $P < .05$) was found, indicating that P50 amplitudes in CP and healthy participants were also differentially modulated by the stimulated body location (Table 2). Post-hoc comparisons revealed that contralateral P50 amplitudes elicited by lip stimulation were more reduced in children with CP than in healthy children ($P < .05$). Moreover, contralateral P50 amplitudes elicited by thumb stimulation were more enhanced in healthy children than in healthy adults ($P < .05$), whereas no age-related differences were observed in participants with CP.

3.2.2. Mean P100 amplitude

A significant three-way interaction of BRAIN HEMISPHERE × AGE × PATIENT GROUP ($F(1,55) = 5.34$, $P < .05$) was yielded, indicating that P100 amplitudes were modulated by age in healthy, but not in CP participants. Post-hoc pairwise comparisons showed that P100 amplitudes over the contralateral hemisphere were more increased in healthy children than in healthy adults ($P < .05$), whereas no age-related differences appeared in participants with CP. Post-hoc comparisons further showed that P100 amplitudes were more enhanced over the contralateral hemisphere in adults with CP than in healthy adults ($P < .05$), whereas no group differences were observed in children.

In addition, a four-way interaction of BODY LOCATION × STIMULATION SIDE × AGE × PATIENT GROUP ($F(1,55) = 6.22$, $P < .05$) was also significant. Post-hoc pairwise comparisons further revealed that P100 amplitudes elicited by stimulation of lip and thumb were more increased on the right than on the left hemisphere in participants with CP ($P < .05$), whereas no brain asymmetries were observed in healthy participants (Table 2). Moreover, it was found that P100 amplitudes elicited by stimulation of the right lip elicited were more reduced in children with CP than in healthy children ($P < .05$), and that P100 amplitudes elicited by stimulation of the left thumb were more increased in adults with CP than in healthy adults ($P < .05$).

4. Discussion

We found that individuals with cerebral palsy (CP) displayed an abnormal processing of information arising from the body including proprioception, touch sensitivity and pain pressure thresholds, as well as somatosensory evoked potentials elicited by non-painful stimuli. Interestingly, most differences between individuals with CP and healthy controls appeared when age was taken into account. Thus, children with CP showed more reduced touch sensitivity and enhanced pain sensitivity than healthy children, but no differences appeared when adults with CP and healthy were compared. Moreover, children with CP displayed higher touch sensitivity on the lip than on the thumb, as it occurred in healthy controls, but no differences were observed in adults with CP. With respect to brain activity, group differences on P50 and P100 amplitudes between participants with CP and healthy were also found in children, and not in adults. Moreover, healthy children showed higher SEP amplitudes than healthy adults, whereas no differences between children and adults with CP were observed. Finally, significant hemispheric asymmetries of P100 amplitudes were found in CP when left and right-side body parts were stimulated.

Our data of an abnormal somatosensory sensitivity in children with CP are in agreement with previous research, showing that stereognosis and proprioception were also strongly reduced as compared with healthy children (Cooper et al., 1995; Sanger and Kukke, 2007; Wingert et al., 2009), and that touch hyposensitivity could be linked to increased pain sensitivity in children with early injury (Schmelzle-Lubiecki et al., 2007). In the present study, we extend those results, showing that children with CP displayed more reduced touch sensitivity together with more enhanced pain sensitivity in the lip area as compared with healthy. The finding of higher pain sensitivity in children with CP is also of particular importance, since pain has been identified as a major health concern in cerebral palsy (Vogtle, 2009). We have previously observed that children with CP reported more pain than healthy participants, and that pain was experienced as chronic in 45% of participants with CP (Riquelme & Montoya, personal communication). In this sense, it has been suggested that movement impairments (joint deformity, spasticity, muscle weakness) that characterize CP might lead to a high incidence of pain experience among this population (Vogtle, 2009). Moreover, the regular participation of children with CP in chirurgic and rehabilitation procedures (stretching, electrical stimulation, functional mobility training, splinting and orthotic fabrication, serial casting, training for use of adaptive equipment, and utilization of standing frames and other positioning devices) could be associated with a high prevalence of pain (Brattberg, 2004). In the present study, we observed that participants with CP showed greater pain sensitivity than

Table 2
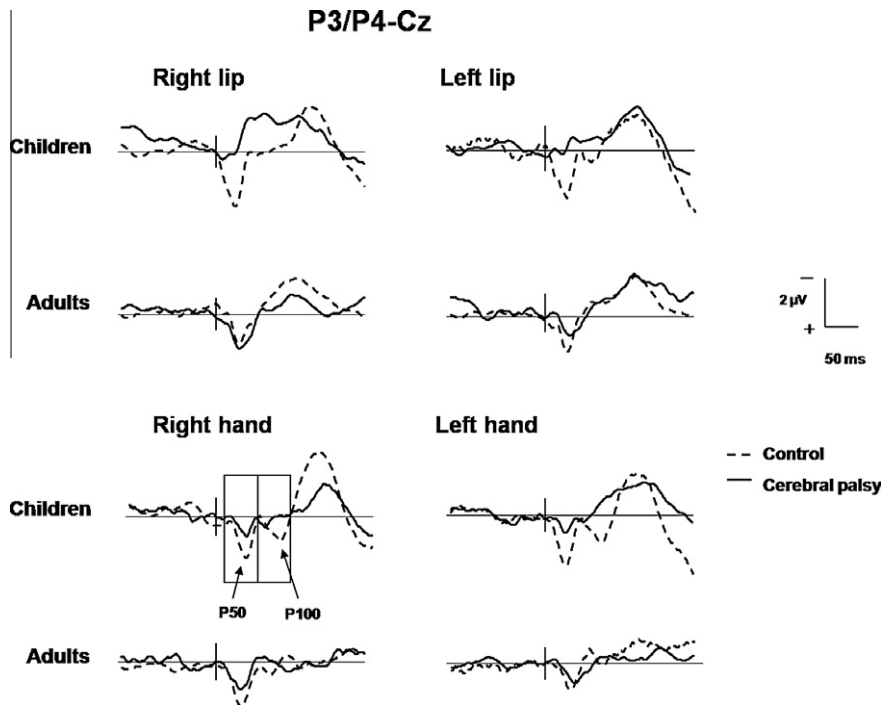Means and standard deviations of somatosensory evoked potentials amplitudes by tactile stimulation of lips and thumbs in cerebral palsy and healthy controls, separated by age group, stimulus location and brain hemisphere.

		Children		Adults	
		Control	CP	Control	CP
P50					
Lip	Right ipsilateral	0.51 (0.72)	−0.13 (1.15)	0.02 (0.83)	0.45 (0.69)
	Right contralateral	1.12 (0.88)	0.62 (1.27)	0.49 (0.53)	0.63 (0.71)
	Left ipsilateral	0.42 (0.98)	−0.15 (0.71)	0.42 (0.49)	0.13 (0.54)
	Left contralateral	1.14 (0.88)	0.38 (1.10)	0.74 (0.54)	0.77 (0.94)
Thumb	Right ipsilateral	−0.35 (0.64)	0.27 (1.31)	0.14 (0.57)	0.08 (1.09)
	Right contralateral	1.46 (1.22)	0.62 (1.45)	0.37 (0.50)	0.50 (1.18)
	Left ipsilateral	−0.20 (0.95)	0.01 (1.54)	0.20 (0.52)	−0.60 (2.36)
	Left contralateral	1.70 (1.29)	0.80 (1.12)	0.40 (0.45)	0.89 (1.69)
P100					
Lip	Right ipsilateral	0.29 (0.94)	−0.06 (1.24)	−0.32 (1.06)	0.29 (0.82)
	Right contralateral	0.35 (0.95)	−0.48 (0.98)	−0.71 (0.87)	−0.01 (0.96)
	Left ipsilateral	−0.37 (1.32)	−0.04 (1.21)	−0.04 (0.38)	−0.28 (0.92)
	Left contralateral	0.31 (1.13)	−0.04 (1.67)	−0.58 (0.84)	0.55 (1.80)
Thumb	Right ipsilateral	−0.34 (1.36)	0.01 (1.93)	0.12 (0.60)	0.49 (1.84)
	Right contralateral	0.89 (1.16)	−0.33 (1.98)	−0.22 (0.80)	−0.10 (1.31)
	Left ipsilateral	−0.29 (0.96)	−0.44 (1.21)	0.02 (0.69)	0.16 (0.86)
	Left contralateral	1.25 (0.98)	−0.45 (1.72)	−0.71 (0.82)	0.46 (2.76)

healthy on the lip, but not on the digit. Similarly, group differences in touch sensitivity and brain activity appeared mostly on the lip, suggesting the possibility that plastic changes occurring in somatosensory cortices would be modulating the differences in touch and pain sensitivity. All these findings are basically consistent with results of human and animal studies indicating that early infant injury has not only local, but also global long-term consequences upon sensory processing (Schmelzle-Lubiecki et al., 2007).

In the present study, we also observed that somatosensory brain responses to non-painful stimulation were significantly altered in CP compared to healthy. Basically, P50 and P100 amplitudes were more enhanced in children and adults with CP than in healthy participants. Moreover, these early amplitudes of the somatosensory evoked potentials (SEP) were modulated by age in healthy controls, but not in participants with CP. Nevertheless, we also found that more increased brain responses were elicited when the left body area was stimulated as compared to the right one in children and adults with CP, whereas brain responses in healthy participants were symmetrical. Further abnormalities in quantitative and coherence EEG over centro-parietal regions have also been reported previously (Kulak and Sobaniec, 2005; Kułak et al., 2006), suggesting changes in the organization of sensory and motor pathways. Thus, it seems plausible that the greater SEP amplitudes elicited by the left-side of the body in the present study were reflecting some kind of cortical reorganization, showing that the injured body side might alter its representation in the contralateral somatosensory cortex. In recent years, several experiments have demonstrated that the human nervous system retains the ability to reorganize itself in response to peripheral changes as it occurs after amputation (Montoya et al., 1998), stroke (Floel et al., 2008), or focal hand dystonia (Elbert et al., 1998). Basically, these studies showed a significant reorganization of somatosensory cortex so that the representation of the mouth area moves into the area normally occupied by the injured extremity. There have been also some results indicating that activity-dependent plasticity could play a role in the evolution of clinical signs of motor dysfunction in children with CP (Eyre, 2007). Thus, our observation that the left-side stimulation elicited greater brain responses than the right-side stimulation raises the intriguing possibility that motor dysfunction in CP could be modulated by an enhanced excitability of somatosensory cortex. Our results are consistent with this possibility and provide initial support for further experiments directed at sensory intervention.

Thus, it seems that although CP is mainly characterized by motor impairments, brain processing of incoming somatosensory information could also be altered in this pathology. According with this view, previous neuroimaging research has found that children born preterm with periventricular leukomalacia showed more severe injury in posterior white matter fibers connecting the thalamus to the sensory cortex than in descending corticospinal tracts (Hoon et al., 2002). More recently, it has been demonstrated that somatosensory processing deficits (reduced touch sensitivity, proprioception and strength) in CP could be related to injury severity in the diffuse thalamocortical projections to the somatosensory and parietal cortex (posterior thalamic radiation) (Coq et al., 2008). An alternative explanation could be that abnormal somatosensory processing observed in the present study could be due to general cognitive deficits which would be affecting the results of the sensitivity tests. In a similar way, epilepsy has been shown to influence somatosensory brain activity (Bast et al., 2007). Considering that a large number of CP patients in this study had epilepsy, one could argue that our results would be also affected by this clinical variable. Nevertheless, further statistical comparisons revealed that no differences were yielded due to epilepsy status or mental retardation in the present study (data not reported here). Thus, it seems that altered functional organization and connectivity of somatosensory brain regions might be relevant for explaining motor impairments in CP.

Our study has some limitations which should be taken into account for the interpretation of the results. First, although our sample of persons with CP seems to be representative of the large population in our community, the sample size was small and the type of cerebral palsy and location of cerebral injury was quite heterogeneous. The inclusion of children and adults in the sample was not representative of the all lifespan, and individuals younger than 5 or adolescents between 15 and 20 years were not included. Somatosensory evoked potentials provide information from the cortical grey matter, thus the influence of subcortical structures (thalamus) in somatosensory processing remains underexplored. Finally, the cross-sectional design of the present study represents a further limitation. Although our study does not provide information about how the somatosensory processing is changing over the time in CP, it lays the scientific basis for implementation of a longitudinal design and guides the selection of appropriate outcome measures for future studies.

All these findings highlight the importance of considering the presence of pain and somatosensory deficits in cerebral palsy at a very early age, and the need to specifically assess sensitivity functions and address rehabilitation programs throughout the lifespan, which should include not only sensoriomotor therapy but also biopsychosocial interventions for pain relief. Thus, considering the interactions between somatosensory information processing and motor function, as well as the fact that somatosensory training may help to improve motor deficits (Floel et al., 2008; Kaelin-Lang, 2008), it seems plausible that such intervention programs might also be helpful to children and adults with CP. Our results are consistent with this possibility and preliminary research has already provided support for such interventions in children with CP (Bumin and Kayihan, 2001).

Acknowledgements

References

Bast T, Wright T, Boor R, Harting I, Feneberg R, Rupp A, et al. Combined EEG and MEG analysis of early somatosensory evoked activity in children and adolescents with focal epilepsies. Clin Neurophysiol 2007;118(8):1721–35.

Brattberg G. Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 2004;8:187–99.

Bumin G, Kayihan H. Effectiveness of two different sensory-integration programmes for children with spastic diplegic cerebral palsy. Disabil Rehabil 2001;23(9):394–9.

Cathcart S, Pritchard D. Reliability of pain threshold measurement in young adults. J Headache Pain 2006;7(1):21–6.

Clayton K, Fleming JM, Copley J. Behavioral responses to tactile stimuli in children with cerebral palsy. Phys Occup Ther Pediatr 2003;23(1):43–62.

Cooper J, Majnemer A, Rosenblatt B, Birnbaum R. The determination of sensory deficits in children with hemiplegic cerebral palsy. J Child Neurol 1995;10(4):300–9.

Coq JO, Strata F, Russier M, Safadi FF, Merzenich MM, Byl NN, et al. Impact of neonatal asphyxia and hind limb immobilization on musculoskeletal tissues and S1 map organization: Implications for cerebral palsy. Exp Neurol 2008;210:95–108.

Elbert T, Candia V, Altenmuller E, Rau H, Sterr A, Rockstroh B, et al. Alteration of digital representations in somatosensory cortex in focal hand dystonia. Neuroreport 1998;9:3571–5.

Eyre JA. Corticospinal tract development and its plasticity after perinatal injury. Neurosci Biobehav Rev 2007;31(8):1136–49.

Floel A, Hummel F, Duque J, Knecht S, Cohen LG. Influence of somatosensory input on interhemispheric interactions in patients with chronic stroke. Neurorehabil Neural Repair 2008;22(5):477–85.

Hoon AH, Lawrie WT, Melhem ER, Reinhardt EM, Van Zijl PC, Solaiyappan M, et al. Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. Neurology 2002;59(5):752–6.

Hoon AH, Stashinko EE, Nagae LM, Lin DD, Keller J, Bastian A, et al. Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Dev Med Child Neurol 2009;51(9):697–704.

Kaelin-Lang A. Enhancing rehabilitation of motor deficits with peripheral nerve stimulation. NeuroRehabilitation 2008;23(1):89–93.

Keizer D, Fael D, Wierda JM, van Wijhe M. Quantitative sensory testing with Von Frey monofilaments in patients with allodynia: what are we quantifying? Clin J Pain 2008;24(5):463–6.

Kułak W, Sobaniec W, Sołowiej E, Boćkowski L. Somatosensory and visual evoked potentials in children with cerebral palsy: correlations and discrepancies with MRI findings and clinical picture. Pediatr Rehabil 2006;9(3):201–9.

Kulak W, Sobaniec W. Quantitative EEG analysis in children with hemiparetic cerebral palsy. NeuroRehabilitation 2005;20(2):75–84.

Montoya P, Ritter K, Huse E, Larbig W, Braun C, Töpfner S, et al. The cortical somatotopic map and phantom phenomena in subjects with congenital limb atrophy and traumatic amputees with phantom limb pain. Eur J Neurosci 1998;10(3):1095–102.

Montoya P, Sitges C, Garcia-Herrera M, Rodríguez-Cotes A, Izquierdo R, Truyols M, et al. Reduced brain habituation to somatosensory stimulation in patients with fibromyalgia. Arthritis Rheum 2006;54:1995–2003.

Montoya P, Sitges C. Affective modulation of somatosensory evoked potentials elicited by tactile stimulation. Brain Res 2006;1068(1):205–12.

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997;39(4):214–23.

Sanger TD, Kukke SN. Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. J Child Neurol 2007;22(3):289–93.

Schmelzle-Lubiecki BM, Campbell KA, Howard RH, Franck L, Fitzgerald M. Long-term consequences of early infant injury and trauma upon somatosensory processing. Eur J Pain 2007;11(7):799–809.

Thomas B, Eyssen M, Peeters R, Molenaers G, Van Hecke P, De Cock P, et al. Quantitative diffusion tensor imaging in cerebral palsy due to periventricular white matter injury. Brain 2005;128(11):2562–77.

Vogtle LK. Pain in adults with cerebral palsy: impact and solutions. Dev Med Child Neurol 2009;51(4):113–21.

Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Joint-position sense and kinesthesia in cerebral palsy. Arch Phys Med Rehabil 2009;90(3):447–53.

Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Tactile sensory abilities in cerebral palsy: deficits in roughness and object discrimination. Dev Med Child Neurol 2008;50(11):832–8.

Manuscrito:

Differences in the somatosensory processing due to the dominant hemispheric motor impairment in cerebral palsy

DIFFERENCES IN THE SOMATOSENSORY PROCESSING DUE TO THE DOMINANT HEMISPHERIC MOTOR IMPAIRMENT IN CEREBRAL PALSY

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Running title: Somatosensory processing, dominant hemspheric impairment and cerebral palsy

Abstract

Objective. Cerebral palsy (CP) is a motor disorder, which also causes somatosensory deficits. Somatosensory information is essential for correctly planning and executing the movement. The alteration of the somatosensory feedback may be related with the characteristics of the movement impairment. *Methods*. SEP elicited by tactile stimulation in lips and thumbs were examined in 9 persons with CP (range 7-29y) with dominating left motor impairment and 8 persons with CP (range 5-28y) with dominating right motor impairment. *Results*. Both groups displayed higher SEP amplitudes when the most affected motor body side was stimulated on lips in P50. Differences between the groups were found in the hemispheric activation both on hands and lips, in P50 and P100 SEP amplitudes and time-frequency power on the alpha and beta bands. Thus, while RCP usually showed enhanced activation over the contralateral hemisphere to the stimulated body side, LCP either not showed this hemispheric differentiation or showed enhanced activation over the ipsilateral hemisphere to the stimulated body side. *Conclusions*. Data suggest a different somatosensory cortical organization depending on the dominant side of the motor impairment and offer a new approach both to further study of plasticity and to the conception of rehabilitation programs in persons with CP.

Keywords: somatosensory processing, cerebral palsy, motor dominance, hemispheric impairment**.**

INTRODUCTION

Cerebral palsy (CP) has been described as a group of permanent disorders of the development of movement and posture, that are attributed to non-progressive disturbances in the developing fetal or infant brain, and that are often accompanied by disturbances of sensation, perception and secondary musculoskeletal problems among others (Rosenbaum et al., 2006). Research on somatosensory processing has revealed that CP patients are characterized by poor tactile discrimination, stereognosis and proprioception (Wingert et al., 2009; Sanger & Kukke, 2007; Cooper et al., 1995), as well as increased pain (Riquelme et al., 2011) and enhanced activation of cortical somatosensory areas (Riquelme & Montoya, 2010). Moreover, somatosensory parameters have been positively associated with clinical measures of motor impairment in persons with CP and other neurological pathologies such as multiple sclerosis, spinal cord injuries and cerebrovascular accidents (Nociti et al., 2008; Nardone et al., 2008; Park et al., 2003; Platz et al., 2000; Kusoffsky et al., 1982). Neuroimaging studies have also provided evidence of significant alterations in white matter fibers connecting to sensory cortex (radiata and internal capsule), suggesting that CP injuries might be reflecting disruption of sensory as well as motor connections (Hoon et al., 2009; Thomas et al., 2005; Hoon et al., 2002).

Although the neurophysiological mechanisms involved in the altered processing of bodily information in CP are still unknown, there is evidence of abnormalities of sensorimotor integration in hemiplegic CP (Thickbroom et al., 2001), as it occurs in other movement disorders such as Parkinson' disease, Huntington's disease, dystonia, and tics (Lourenço et al., 2007; Schmelzle-Lubiecki et al., 2007, Abbruzzese & Berardelli, 2003). Furthermore, it is known that motor reorganization in children with congenital hemiplegic cerebral palsy can often occur by preserving motor representations of the affected arm in the undamaged ipsilateral hemisphere. In this sense, studies using transcranial magnetic stimulation (TMS) provided evidence of ipsilateral corticospinal projections from the undamaged motor cortex to muscles of the affected hand (Eyre et al., 2001; Thickbroom et al., 2001; Cincotta et al., 2000; Maegaki et al., 1995, 1997; Carr et al., 1993; Farmer et al., 1991). Moreover, it has been proposed that somatosensory deficits could be due to secondary effects provoked by the motor limitation and the reduction of opportunities to explore the environment (Clayton et al., 2003). In this sense, the monotonous and stereotypical patterns of spontaneous movements in patients with hemiplegic cerebral palsy would result in abnormal sensory

feedback and altered cortical reorganization, thus leading to somatosensory processing deficits (Coq et al., 2008; Clayton et al., 2003). A case study by Ragazzoni and colleagues (2002) further showed that somatosensory function of the affected arm (right) was preserved, whereas motor function was poor despite fast-conducting ipsilateral cortico-motoneuronal output from the primary motor cortex of the undamaged hemisphere to the affected arm. This finding seems to suggest that different forms of motor and somatosensory reorganization operate in congenital brain injury, and that fast-conducting connections between primary cortex areas and ipsilateral spinal cord are not sufficient for preservation or recovery of function.

In the present study, we examine the effects of motor impairment on somatosensory brain processing through somatosensory evoked potentials (SEP) elicited by non-painful tactile stimulation among persons with CP. For this purpose, we divide our CP sample into patients with either dominant right-sided or left-sided motor impairments to test if the side of the motor impairment would affect the magnitude and the frequency of the early SEP components.

METHODS

Participants

Eighteen individuals with cerebral palsy (CP) were recruited from educational and occupational centers established in the island of Majorca (Spain), and invited to participate in the study. Persons with CP were classified according to the dominant side of motor impairment into two groups: 1) nine CP participants with right-sided motor impairment (RCP) (3 females; mean age = 18y 3mo, range 5-28y), and 2) nine CP with left-sided motor impairment (LCP) (3 females; mean age 15y 4mo, range 7-29y). Table 1 displays clinical characteristics of participants with cerebral palsy within each group. Subjects or their parents reported their age and sex. The type of cerebral palsy, gestational age, cognitive level, presence of epilepsy and medication were obtained from participant's health history. The level of motor impairment was also determined using the Gross Motor Function Classification Scale (GMFCS) (Palisano et al., 1997).

Participants granted informed consent according with the Declaration of Helsinki. For participants under the age of 18, permission and written informed consent from their parents or legal tutors were obtained. Healthy adults provided written informed consent and verbalized willingness to participate. In the case of adults with CP, their parents or legal tutors provided written informed consent, and participants

verbalized willingness to participate. The study was approved by the Ethics Committee of the Regional Government of the Balearic Islands.

EEG recording and processing

Somatosensory evoked-potentials (SEP) elicited by tactile stimulation at four body locations (right lip, left lip, right hand and left hand) were recorded in a sound attenuated, semi-darkened room. Subjects were seated in a reclining chair and encouraged to relax and to keep their eyes closed. In younger children, mother was allowed to remain in the room if the child was anxious. Non-painful tactile computer-controlled impulses were delivered bilaterally at the body locations using a pneumatic stimulator, consisting of a small membrane attached to the body surface by a plastic clip and fixated with adhesive strips. Each stimulation block consisted of 120 stimuli of 100 ms duration with an approximate pressure of 2 bars and a variable inter-stimulus interval of 1000 ± 50 ms. A similar tactile stimulation has been already used in previous research of our lab to study somatosensory processing in persons with CP (Riquelme & Montoya, 2010). Electrical brain activity was registered with a 20-channels EEG amplifier with electrodes located according with the international 10/20 system and referenced to Cz. Vertical electrooculograms (EOG) were recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 10 kOhm. The sampling rate was set at 1000 Hz and filter bandpass at 0.1-40 Hz. A digital signal from the tactile stimulation device was used as a trigger for SEP acquisition. SEPs were averaged relative to a 150-ms prestimulus baseline. Eye movement artifacts were corrected using Gratton & Coles (1983) algorithm. An artifact rejection protocol with following criteria was applied: 75 μV as maximal allowed voltage step/sampling point; ±75 μV as minimum and maximum allowed amplitudes; and 75 μV as maximum allowed absolute difference. One subject of the RCP subgroup had to be eliminated from statistical analyses because their EEG recordings did not meet the criteria specified above. Finally, EEG waveforms were averaged separately for each body location.

Our previous work has shown that non-painful tactile stimuli evoke a typical SEP waveform with readily identifiable components at several latencies between 50 and 125 ms (Riquelme & Montoya, 2010; Montoya et al., 2006; Montoya & Sitges, 2006). According with these studies and based on visual inspection of the grand-average waveforms, we computed SEP mean amplitudes for two time windows: 20-70 ms (P50) and 70-120 ms (P100) after stimulus onset. Moreover, event-related brain oscillations

elicited by somatosensory stimuli were analyzed by computing the relative increases or decreases of each frequency power with respect to the baseline interval (100 ms before stimulus onset). These time-frequency analyses of evoked power were computed using a Mortlet wavelet (width 7 cycles) by convolution in the frequency domain on single trials over an interval between stimulus onset and 600 ms after stimulus onset. An average absolute power value for each electrode and each body location was calculated separately for following frequency bands: theta (4-8 Hz), alpha (8-12 Hz), and beta (12-30 Hz).

Statistical analyses

Amplitudes and frequency power of the somatosensory-evoked responses over central (C3, C4) and parietal electrodes (P3, P4) were analyzed by using multivariate analyses of variance (MANOVA) with the between-subject factor GROUP (right- vs. left-sided motor impairment), as well as the within-subject factors stimulated BODY SIDE (right vs. left), HEMISPHERE (contralateral vs. ipsilateral to stimulated body side) and BRAIN LOCATION (parietal vs. central). In all cases, interaction effects were assessed using post-hoc mean comparison tests provided by the MANOVA procedure in SPSS.

RESULTS

Amplitude analyses of somatosensory evoked potentials

Amplitude analysis of somatosensory evoked potentials (SEPs) elicited by the stimulation of lip and thumb over the contralateral and ipsilateral hemispheres are shown in Figure 1. Within the first 150-ms interval, SEPs were characterized by a prominent positive peak around 50 ms (P50), followed by a second positive peak around 100 ms after stimulus onset (P100). Although these peaks were clearly observable after thumb stimulation in grand averages, peak detection in individual averages was difficult and, therefore, the mean amplitudes in the two time windows (20-70 ms and 70-120 ms after stimulus onset) were computed and statistically analyzed.

– Please, insert Figure 1 about here –

P50 amplitude. For stimulation of the lips, we observed a significant GROUP x BODY SIDE interaction effect ($F_{(1,15)}=6.2$; $P<.05$), indicating that somatosensory stimulation elicited higher amplitudes when the most impaired lip was stimulated: the

right part of the lip in the case of CP patients with right-sided motor impairment (RCP), and the left part of the lip in the case of CP patients with left-sided motor impairment (LCP) (both Ps<.1). For stimulation of the thumbs, a two-way interaction GROUP x HEMISPHERE (F(1,15)=5.9; P<.05) was observed, showing that RCP displayed higher amplitudes over the left than over the right hemisphere (P<.05); whereas no differences were found in LCP.

P100 amplitude. No significant interactions were observed in the stimulation of the lips. For stimulation of the thumbs, statistical analyses of brain activity confirmed that P100 amplitudes were significantly higher over the contralateral hemisphere than over the ipsilateral hemisphere to the stimulation side (main effect of BRAIN HEMISPHERE: F(1,15)=22.4, P<.001). A main effect of GROUP (F(1,15)= 4.6, P<.05) revealed that RCP displayed higher SEP amplitudes than LCP.

Time-frequency analyses of somatosensory evoked oscillations
Temporal changes in power spectra of the somatosensory evoked oscillations elicited by the stimulation of lip and thumb over the contralateral and ipsilateral hemispheres are shown in Figure 2.

− Please, insert Figure 2 about here −

For stimulation of the lips, we observed a significant GROUP x HEMISPHERE interaction effect on the power of alpha frequency band (F(1,15)=6.6, P<.05), indicating that somatosensory stimulation elicited differential brain activation over the hemispheres depending on the groups. Post-hoc mean comparisons indicated that alpha power over the ipsilateral hemisphere was higher in persons with LCP than with RCP (P<.05); whereas no group differences were observed over the contralateral hemisphere. No significant differences between the groups were found in the beta and theta bands.

For stimulation of the thumbs, a three-way interaction GROUP x HEMISPHERE x BODY SIDE (F(1,15)=8.2; P<.05) was observed in the beta frequency band. Post-hoc mean comparisons indicated that persons with RCP displayed more enhanced beta power over the contralateral hemisphere than over the ipsilateral hemisphere (right) after stimulation of the healthy thumb (left) in persons with RCP

(P<.01), but no hemispheric differences were yielded after stimulation of the affected thumb, or in persons with LCP. No significant differences between the groups were found in the alpha and theta bands when thumbs were stimulated.

DISCUSSION

This study was aimed to evaluate the effects of motor impairment on brain processing of non-painful tactile stimulation in persons with cerebral palsy (CP). Our findings revealed that both groups of CP patients with right- (RCP) and left-sided motor impairment (LCP) displayed higher amplitudes in the early latencies of the somatosensory evoked potentials (SEP) when the most impaired motor body side was stimulated. Nevertheless, a differential activation of the contralateral and ipsilateral hemispheres was observed in the two groups of CP patients. Thus, RCP patients showed more enhanced activation over the contralateral hemisphere to the stimulated body side, whereas LCP patients showed either no hemispheric differentiation or an enhanced activation over the ipsilateral hemisphere to the stimulated body side.

Our results revealed altered somatosensory processing in individuals with CP, both in SEP amplitudes and frequency mean power. These results are in agreement with previous literature showing that, although CP is mainly characterized by motor impairments, brain processing of incoming somatosensory information is also altered in this pathology. According with this view, previous neuroimaging research has found that children born preterm with periventricular leukomalacia showed more severe injury in posterior white matter fibers connecting the thalamus to the sensory cortex than in descending corticospinal tracts (Hoon et al., 2002). It has also been demonstrated that somatosensory processing deficits (reduced touch sensitivity, proprioception and strength) in CP could be related to injury severity in the diffuse thalamocortical projections to the somatosensory and parietal cortex (Coq et al, 2008). Our results confirm the complex nature of CP pathology and highlight the importance of somatosensory deficits on persons with CP.

An asymmetry of the motor function is often observed, even in individuals with bilateral CP (Bourelle et al., 2010; Descatoire et al., 2010; Park et al., 2006). This asymmetry has been observed in physiological measures such as nerve conduction velocities or listening processing (Kalizhniuk & Fedorchuk, 1985; Lang et al., 1983). In our sample of CP, we found enhanced early SEP amplitudes (P50) when the most affected body side was stimulated. It seems possible that the greater SEP amplitudes

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elicited by the more affected side of the body in the present study were reflecting some kind of cortical reorganization, showing that the injured body side might alter its representation in the contralateral somatosensory cortex. In recent years, several studies have demonstrated that the human nervous system retains the ability to reorganize itself in response to peripheral changes as it occurs after amputation (Montoya et al., 1998), stroke (Floel et al., 2008), or focal hand dystonia (Elbert et al., 1998). Basically, these studies showed a significant reorganization of somatosensory cortex so that the representation of the mouth area moves into the area normally occupied by the injured extremity. Our results are consistent with the possibility of reorganization of the somatosensory primary cortical areas as result of early motor impairment.

In addition to this asymmetric organization of the somatosensory areas, we also found differences in the hemispheric activation depending on the right or left dominant motor impairment. In this way, RCP seem to reproduce a more normal contralateral activation pattern, but LCP either did not showed differences between hemispheric activation or even showed increased ipsilateral activation to the stimulated side. The unusual pattern of bilateral cortical activation and the recruitment of ipsilateral tracts have been considered as a reflect of widespread alternative cortical organisation (Krägeloh-Mann & Canns, 2009; Eyre et al., 2007; Briellmann et al., 2002; Maegaki et al., 1999). The capital influence of the side of the lesion in motor functions has been reported in unilateral CP lesions. Van Kampen and colleagues (2010) reported that children with left hemiparesis needed a longer decision time when asked to intercept a ball and started their reach movement earlier than healthy controls and children with right hemiparesis. Also Craje and colleagues (2009) observed difficulties in switching between different grip types in children with right hemiparesis while participants with left hemiparesis showed consistent planning of the first part of the task. Our findings support the hypothesis that these differences between right-impaired and left-impaired CP can be found also on the somatosensory system and, most interestingly, in the bilaterally motor impaired CP who clinically show a dominance of the motor injury in one of their body sides. This hypothesis is supported by neurophysiological studies which showed higher intrahemispheric coherence for the delta, beta and theta bands in the left hemisphere of chidren with spastic diplegia (Koeda & Takeshita, 1998). These results may open an interesting research area on the study of the nature of the plasticity mechanisms that are developed after early brain injuries and led to new approaches to rehabilitation both of the motor and somatosensory system.

Our study has some limitations which should be taken into account for the interpretation of the results. First, although our sample of persons with CP seems to be representative of the large population in our community, the sample size was small and heterogeneous. Somatosensory-evoked potentials provide information from the cortical grey matter, thus the influence of subcortical structures in somatosensory processing remains underexplored. Nevertheless, our study lays the scientific basis for implementation of further research on a scarcely investigated topic.

These findings suggest a different somatosensory cortical organization depending on the asymmetry of the motor impairment and offer a new approach to study plasticity on the developing brain. Considering that activity-dependent plasticity could play a role in the evolution of clinical signs of motor dysfunction in children with CP (Eyre, 2007) and that interventions are effective to alter the organization of primary somatosensory system (Flor, 2003), these results could also lead to new approaches to a more personalized rehabilitation interventions in persons with CP.

REFERENCES

Abbruzzese G, Berardelli A. Sensorimotor integration in movement disorders. Mov Disord. 2003;18(3):231-40.

Bourelle S, Berge B, Gautheron V, Cottalorda J. Computerized static posturographic assessment after treatment of equinus deformity in children with cerebral palsy. J Pediatr Orthop B. 2010;19(3):211-20.

Carr LJ, Harrison LM, Evans AL, Stephens JA. Patterns of central motor reorganization in hemiplegic cerebral palsy. Brain. 1993;116 (Pt 5):1223-47.

Cincotta M, Borgheresi A, Guidi L, Macucci M, Cosottini M, Lambruschini P, Benvenuti F, Zaccara G. Remote effects of cortical dysgenesis on the primary motor cortex: evidence from the silent period following transcranial magnetic stimulation. Clin Neurophysiol. 2000;111(8):1340-5.

Clayton K, Fleming JM, Copley J. Behavioral responses to tactile stimuli in children with cerebral palsy. Phys Occup Ther Pediatr. 2003;23(1):43-62.

Cooper J, Majnemer A, Rosenblatt B, Birnbaum R. The determination of sensory deficits in children with hemiplegic cerebral palsy. J Child Neurol. 1995;10(4):300-9.

Coq JO, Strata F, Russier M, Safadi FF, Merzenich MM, Byl NN, Barbe MF. Impact of neonatal asphyxia and hind limb immobilization on musculoskeletal tissues and S1 map organization: implications for cerebral palsy. Exp Neurol. 2008;210(1):95-108.

Crajé C, van der Kamp J, Steenbergen B. Visual information for action planning in left and right congenital hemiparesis. Brain Res. 2009;1261:54-64.

Descatoire A, Femery V, Potdevin F, Moretto P. Step-to-step reproducibility and asymmetry to study gait auto-optimization in healthy and cerebral palsied subjects. Ann Phys Rehabil Med. 2009;52(4):319-29.

Elbert T, Candia V, Altenmüller E, Rau H, Sterr A, Rockstroh B, Pantev C, Taub E. Alteration of digital representations in somatosensory cortex in focal hand dystonia. Neuroreport. 1998;9(16):3571-5.

Eyre JA, Smith M, Dabydeen L, Clowry GJ, Petacchi E, Battini R, Guzzetta A, Cioni G. Is hemiplegic cerebral palsy equivalent to amblyopia of the corticospinal system? Ann Neurol. 2007;62(5):493-503.

Eyre JA. Corticospinal tract development and its plasticity after perinatal injury. Neurosci Biobehav Rev. 2007;31(8):1136-49.

Farmer SF, Harrison LM, Ingram DA, Stephens JA. Plasticity of central motor pathways in children with hemiplegic cerebral palsy. Neurology. 1991;41(9):1505-10.

Floel A, Hummel F, Duque J, Knecht S, Cohen LG. Influence of somatosensory input on interhemispheric interactions in patients with chronic stroke. Neurorehabil Neural Repair. 2008;22(5):477-85.

Flor H. Remapping somatosensory cortex after injury. Adv Neurol. 2003;93:195-204.

Gratton G, Coles MG, Donchin E. A new method for off-line removal of ocular artifact. Electroencephalogr Clin Neurophysiol. 1983;55(4):468-484.

Hoon AH Jr, Lawrie WT Jr, Melhem ER, Reinhardt EM, Van Zijl PC, Solaiyappan M, Jiang H, Johnston MV, Mori S. Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. Neurology. 2002;59(5):752-6.

Kalizhniuk ES, Fedorchuk AG. Functional asymmetry of the cerebral hemispheres in infantile cerebral palsy (according to dichotic listening data). Zh Nevropatol Psikhiatr Im S S Korsakova. 1985;85(10):1464-8.

Krägeloh-Mann I, Cans C. Cerebral palsy update. Brain Dev. 2009;31(7):537-44.

Kusoffsky A, Wadell I, Nilsson B. The relationship between sensory impairment and motor recovery in patients with hemiplegia. Scand J Rehabil Med. 1982;14(1):27-32.

Lang AH, Sillanpää M, Hynninen P. Asymmetric function of peripheral nerves in children with cerebral palsy. Acta Neurol Scand. 1983;67(2):108-13.

Lourenço G, Meunier S, Vidailhet M, Simonetta-Moreau M. Impaired modulation of motor cortex excitability by homonymous and heteronymous muscle afferents in focal hand dystonia. Mov Disord. 2007;22(4):523-7

Macnicol MF, Nadeem RD. Evaluation of the deformity in club foot by somatosensory evoked potentials. J Bone Joint Surg Br. 2000;82(5):731-5.

Maegaki Y, Yamamoto T, Takeshita K. Plasticity of central motor and sensory pathways in a case of unilateral extensive cortical dysplasia: investigation of magnetic resonance imaging, transcranial magnetic stimulation, and short-latency somatosensory evoked potentials. Neurology. 1995;45(12):2255-61

Maegaki Y, Maeoka Y, Ishii S, Shiota M, Takeuchi A, Yoshino K, Takeshita K. Mechanisms of central motor reorganization in pediatric hemiplegic patients. Neuropediatrics. 1997;28(3):168-74

Montoya P, Ritter K, Huse E, Larbig W, Braun C, Töpfner S, Lutzenberger W, Grodd W, Flor H, Birbaumer N. The cortical somatotopic map and phantom phenomena in subjects with congenital limb atrophy and traumatic amputees with phantom limb pain. Eur J Neurosci. 1998;10(3):1095-102.

Montoya P, Sitges C, García-Herrera M, Rodríguez-Cotes A, Izquierdo R, Truyols M, Collado D. Reduced brain habituation to somatosensory stimulation in patients with fibromyalgia. Arthritis Rheum. 2006;54(6):1995-2003.

Montoya P, Sitges C. Affective modulation of somatosensory-evoked potentials elicited by tactile stimulation. Brain Res. 2006;1068(1):205-12.

Nardone R, Golaszewski S, Bergmann J, Venturi A, Prünster I, Bratti A, Ladurner G, Tezzon F. Motor cortex excitability changes following a lesion in the posterior columns of the cervical spinal cord. Neurosci Lett. 2008;434(1):119-23.

Nociti V, Batocchi AP, Bartalini S, Caggiula M, Patti F, Profice P, Quattrone A, Tonali P, Ulivelli M, Valentino P, Virdis D, Zappia M, Padua L. Somatosensory evoked potentials reflect the upper limb motor performance in multiple sclerosis. J Neurol Sci. 2008;273(1-2):99-102.

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 1997; 39(4): 214-23.

Park BK, Chae J, Lee YH, Yang G, Labatia I. Median nerve somatosensory evoked potentials and upper limb motor function in hemiparesis. Electromyogr Clin Neurophysiol. 2003;43(3):169-79

Park ES, Kim HW, Park CI, Rha DW, Park CW. Dynamic foot pressure measurements for assessing foot deformity in persons with spastic cerebral palsy. Arch Phys Med Rehabil. 2006;87(5):703-9

Platz T, Kim IH, Pintschovius H, Winter T, Kieselbach A, Villringer K, Kurth R, Mauritz KH. Multimodal EEG analysis in man suggests impairment-specific changes in movement-related electric brain activity after stroke. Brain. 2000;123 Pt 12:2475-90.

Ragazzoni A, Cincotta M, Borgheresi A, Zaccara G, Ziemann U. Congenital hemiparesis: different functional reorganization of somatosensory and motor pathways. Clin Neurophysiol. 2002;113(8):1273-8.

Riquelme I, Montoya P. Developmental changes in somatosensory processing in cerebral palsy and healthy individuals. Clin Neurophysiol. 2010;121(8):1314-20.

Riquelme I, Cifre I, Montoya P. Age-related changes of pain experience in cerebral palsy and healthy individuals. Pain Med. 2011;12(4):535-45.

Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, Dan B, Jacobsson B. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl. 2007;109:8-14.

Russell, D., Rosenbaum, P., Cadman, D., Gowland, C., Hardy, S., Jarvis, S. The gross motor function measure: A means to evaluate the effects of physical therapy. Dev Med Child Neurol. 1989;31,341-352.

Sanger TD, Kukke SN. Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. J Child Neurol. 2007;22(3):289-93.

Schmelzle-Lubiecki BM, Campbell KA, Howard RH, Franck L, Fitzgerald M. Long-term consequences of early infant injury and trauma upon somatosensory processing. Eur J Pain. 2007;11(7):799-809.

Thickbroom GW, Byrnes ML, Archer SA, Nagarajan L, Mastaglia FL. Differences in sensory and motor cortical organization following brain injury early in life. Ann Neurol. 2001;49(3):320-7.

Thomas B, Eyssen M, Peeters R, Molenaers G, Van Hecke P, De Cock P, Sunaert S. Quantitative diffusion tensor imaging in cerebral palsy due to periventricular white matter injury. Brain. 2005;128(Pt 11):2562-77.

Van Kampen PM, Ledebt A, Deconinck FJ, Savelsbergh GJ. Visual guidance of interceptive actions in children with spastic unilateral cerebral palsy is influenced by the side of the lesion. Disabil Rehabil. 2010;32(18):1527-37.

Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Joint-position sense and kinesthesia in cerebral palsy. Arch Phys Med Rehabil. 2009;90(3):447-53.

FIGURE LEGENDS

Table I. Clinical characteristics of individuals with cerebral palsy. (R=right, L=left M=male, F=female, BS=bilateral spastic, D=dyskinetic and A=ataxic).

Figure 1. Amplitude analysis of somatosensory evoked potentials (SEPs) elicited by the stimulation of lip and thumb over the contralateral and ipsilateral hemispheres in each group (dominating right motor impairment –RCP- vs. dominating right motor impairment –LCP-).

Figure 2. Time-frequency analysis of somatosensory evoked potentials (SEPs) elicited by the stimulation of lip and thumb over the contralateral and ipsilateral hemispheres in each group (dominating right motor impairment –RCP- vs. dominating right motor impairment –LCP-).

Table I.

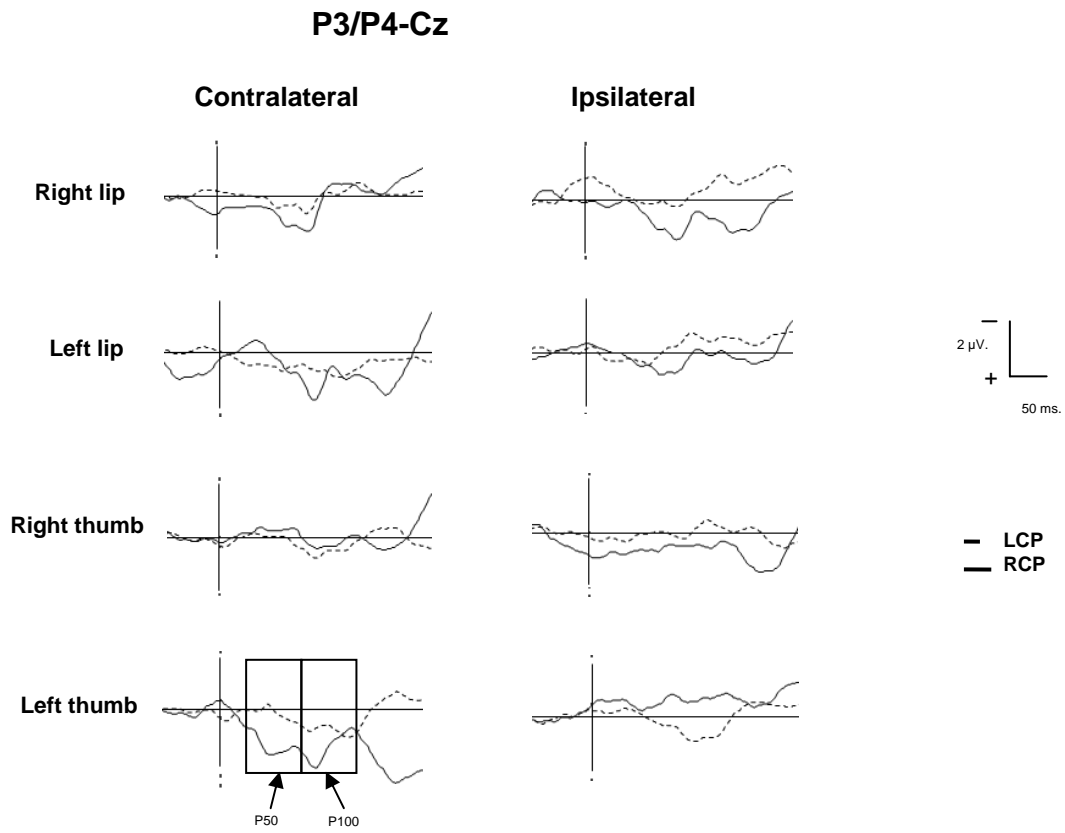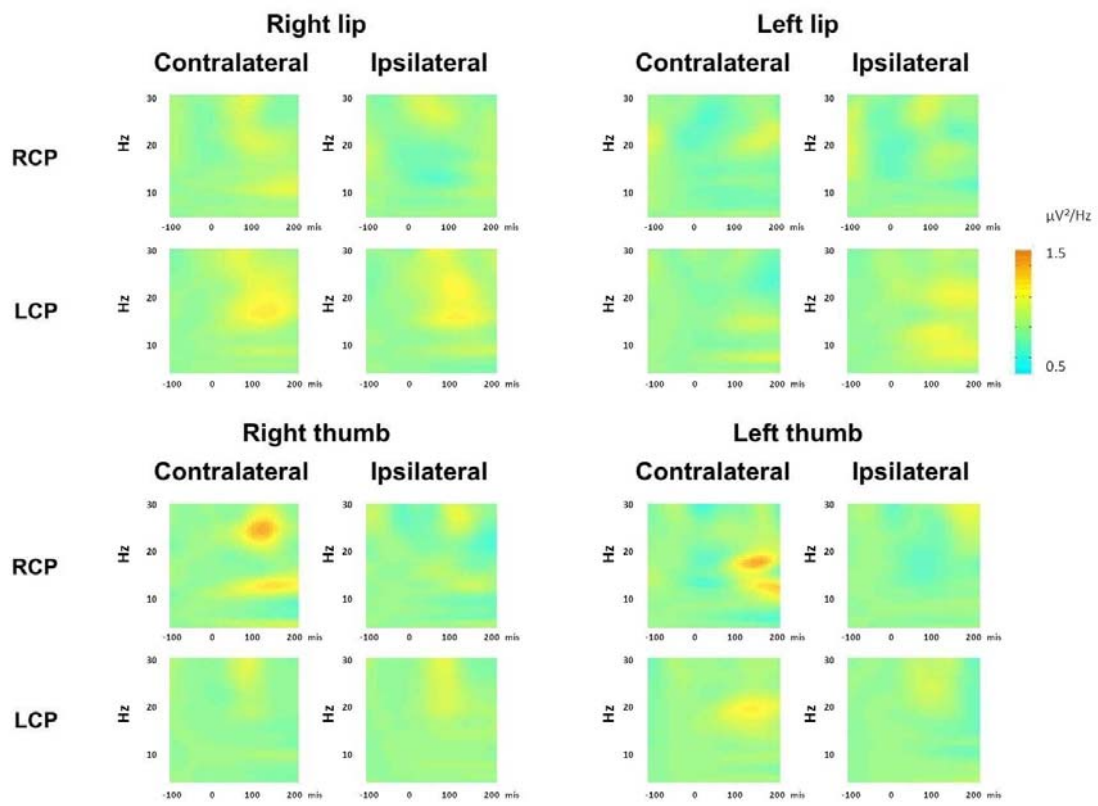| ID	Dominant motor impairment	Sex	Age	CP subgroup	Gestational age(weeks)	GMFCS	Mental retardation	Epilepsia	Medication
1	R	F	12	BS	36	2	No	Yes	Antiepileptic
2	R	F	12	A	40	4	No	No	No
3	R	M	21	A	40	1	Moderate	No	No
4	R	F	11	BS	28	2	No	No	No
5	R	M	5	BS	40	1	No	No	No
6	R	M	28	BS	40	1	Severe	No	Antidepressive
7	R	M	28	A	40	2	Severe	Yes	No
8	R	M	26	BS	40	1	Moderate	No	No
9	R	M	15	BS	32	2	No	No	No
10	L	F	7	BS	20	4	Mild	Yes	Antiepileptic
11	L	M	7	BS	24	1	No	No	Musc. relaxant
12	L	M	9	BS	40	2	Moderate	Yes	Antiepileptic
13	L	M	9	BS	41	3	No	No	No
14	L	M	12	BS	31	3	Mild	No	Antidepressive
15	L	F	7	BS	40	3	No	Yes	Antiepileptic
16	L	M	27	BS	40	1	Moderate	No	No
17	L	M	27	BS	40	3	Moderate	No	No
18	L	F	29	D	42	5	No	Yes	Antidepressive

Figure 1.

P3/P4-Cz

Contralateral   **Ipsilateral**

Right lip

Left lip

2 µV.
+
50 ms.

Right thumb

— LCP
— RCP

Left thumb

P50   P100

Figure 2.

Experimento 3. Procesamiento de la acción motora en las personas con parálisis cerebral.

Presentación de la investigación

Tras comprobar la existencia de trastornos sensitivos en las personas con parálisis cerebral y estudiar tanto su sociodemografía como su procesamiento cortical, nuestro último paso había sido comprobar si la lateralidad de estos trastornos se relacionaba con el hemicuerpo de mayor afectación motora. En esta fase de la investigación, nos planteamos profundizar en el procesamiento del acto motor en personas con parálisis cerebral que presentaban déficits de la sensibilidad dolorosa y somestésica. Para ello, seleccionamos una submuestra de sujetos con parálisis cerebral y de sujetos controles de la misma edad, provenientes de nuestra muestra anterior de sujetos, y les pedimos realizar una acción motriz consistente en la contracción de determinados músculos ante una señal visual y acústica. Nuestro objetivo era comprobar en que fase del movimiento voluntario las personas con parálisis cerebral exhibían alteraciones en el procesamiento motor. Para ello, analizamos las características de la señal electromiográfica (EMG), la amplitud de los potenciales evocados motores (MEP) y la sincronización que presentaba la señal electromiográfica con el EMG (coherencia corticomuscular) en las bandas de frecuencia clásicamente asociadas con el acto motor: alfa y beta (alfa 8-12.99 Hz., beta 15-29.99 Hz.). Como nuestro objetivo era comprobar en que fase de la acción motora se producían las mayores alteraciones, optamos por analizar por separado tres ventanas temporales: el periodo pre-contracción, el periodo de contracción y el periodo post-contracción muscular. La literatura había demostrado un mayor reclutamiento del hemisferio ipsilateral y una coherencia interhemisférica disminuída en los actos motores voluntarios de personas con parálisis cerebral (Krägeloh-Mann & Canns, 2009; Kulak et al., 2005; Briellmann et al., 2002; Maegaki et al, 1999). Nuestros resultados mostraron un aumento de la latencia y duración de la contracción muscular, así como alteraciones en el procesamiento cerebral del acto motor (principalmente, en el periodo pre-contracción) en las personas con parálisis cerebral comparado con los controles sanos. Dada la importancia de las aferencias sensitivas en la planificación del acto motor voluntario, es posible que las alteraciones somatosensoriales y propioceptivas presentes en la población con parálisis cerebral interfieran en la planificación y posterior ejecución de sus movimientos. Esta investigación sienta las bases para, en el futuro,

diseñar estudios que relacionen de forma directa déficits somatosensoriales y propioceptivos con el procesamiento y ejecución motriz. Los resultados del análisis del procesamiento cerebral de este experimento, puede leerse en el manuscrito que se adjunta a continuación.

Manuscrito:

Corticomuscular coherence and muscular evoked potentials indicate impairments in the precontraction time in cerebral palsy compared to healthy individuals

CORTICOMUSCULAR COHERENCE AND MUSCULAR EVOKED POTENTIALS INDICATE IMPAIRMENTS IN THE PRECONTRACTION TIME IN CEREBRAL PALSY COMPARED TO HEALTHY INDIVIDUALS

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Running title: Motor contraction, motor evoked potentials, corticomotor coherence and cerebral palsy.

Abstract

Objective. Cerebral palsy (CP) results of an early lesion in the developing brain, characterized mainly for motor impairments. Deficits on cortical organization of planning and execution of voluntary movements may be one of the causes of the different motor impairments in CP. The objective of this study is to investigate the peripheral and brain process associated to voluntary movements in adults with CP as compared with healthy adults ***Methods***. EMG, MEPs and corticomuscular coherence in alpha and beta bands, elicited by muscular contraction of lateral epicondyles and quadriceps of both sides of the body, were examined in two time intervals (pre-contraction and beginning of the contraction) in 14 persons with CP and 17 healthy controls. ***Results***. Persons withCP as compared with healthy controls showed longer muscular reaction time and duration of the muscular contraction. MEPs amplitudes were significantly enhanced in persons with CP in the pre-contraction time interval.Corticomuscular coherence showed significant lower scores in the pre-contraction time interval, both in the alpha and beta frequency bands, in persons with CP. Moreover, while healthy controls showed a decrease of the corticomuscular coherence between the pre-contraction and contraction intervals, PC subjects showed an increase of this coherence. ***Conclusions***. Our results reaffirm the usefulness ofelectrophysiological parameters for the study of brain impairments and plasticity of de developing central nervous system, as well as a reliable tool to measure rehabilitation efficacy in persons with CP.

Keywords: motor contraction, motor evoked potentials, corticomotor coherence and cerebral palsy

INTRODUCTION

Motor impairment in persons with CP affects both the muscular contraction and the motor central processing. It has been proven that children with CP have reduced voluntary-contraction force, relaxation rate and increased time to produce and reduce movements (Downing et al, 2009; Tammik et al., 2008). On the other hand, the brain lesion affects different structures of the central nervous system producing changes in the motor homunculus, abnormalities in the motor pathways and dysfunction of motor central structures and intracortical connexions (Wittenberg GF., 2009; Hoon et al., 2009; Burton et al., 2009).

Plasticity of the motor system after brain structure injuries has been proven in other pathologies to be a lifelong ability. Studies with stroke patients have showed the displacement of brain activation and an increased need for excitatory drive of pyramidal cells in motor and premotor areas and prolonged conduction time in the affected side (Meng et al, 09; Platz et al., 2000). Studies with hereditary spastic paraparesis found decreased motor-evoked potentials (MEP) and diminished conduction velocity for the lower limbs (Sartucci et al, 2007; Pelosi et al., 1991). In CP, most of the studies of motor plasticity have been addressed to individuals with unilateral brain lesions. Reorganization following unilateral lesions is been proved to be mainly interhemispheric and homotopic. Focusing in the motor system, it was associated to an unusual pattern of bilateral cortical activation that would involve the recruitment of ipsilateral tracts (Krägeloh-Mann &Canns, 2009; Briellmann et al., 2002, Kulak et al., 2005). The scarce research with bilateral lesions also showed a reinforcement of ipsilateral motor pathways in both spastic and athetoid CP (Maegaki et al, 1999) and a decreased EEG coherence in patients with agenesis of the corpum callosum (Kulak et al., 2005).

This study aims to contribute to the knowledge of the physiological mechanisms of motor cortex plasticity after bilateral cerebral lesions in adults with cerebral palsy. The analysis of cerebral electro-physiological activity during the course of planning or execution of movement could reveal interesting information about the brain functional organization in individuals with CP. We investigated central motor planification and execution of the muscular contraction for lateral epicondyles and quadriceps muscles in adults with bilateral CP compared with healthy adults, analyzing the characteristics of MEP and corticomuscular coherence, as long as the characteristics of muscular contraction.

METHODS

Participants

Fourteen persons with CP recruited in occupational centers of Mallorca (4 females; mean age 29y 3mo, SD 12y 8mo), and 17 healthy controls (2 females; mean age 25y 11mo, SD 8y 1mo), were invited to participate in this study. Subjects were selected based on the following criteria: a) age over 14 years, b) bilateral CP (for CP volunteers). Type of cerebral palsy, prematurity, cognitive level and location of cerebral impairment were obtained from the health history and level of motor impairment was determined using the Gross Motor Function Classification Scale (GMFCS) (Palisano et al., 1997). Table 1 displays clinical characteristics of participants with cerebral palsy within each age group.

– Please, insert Table 1 about here –

Participants granted informed consent according with the Declaration of Helsinki. For participants under the age of 18, permission and written informed consent from their parents or legal tutors were obtained. Healthy adults provided written informed consent and verbalized willingness to participate. In the case of adults with CP, their parents or legal tutors provided written informed consent, and participants verbalized willingness to participate. The study was approved by the Ethics Committee of the Regional Government of the Balearic Islands.

Experimental paradigm

Participants were seated in a dimly lit, sound-attenuated room in front of a computer screen. Firstly, participants were oriented to the task and recording procedures. Electrodes were attached to participant´s muscles (lateral epicondyles and quadriceps on both sides) and scalp. The subject was instructed to execute a knee extension and open-and-close task for the hand, as fast as possible and with maximum contraction and to release it as fast as possible when a visual and acoustic signal was presented in computer screen. The experimental session consisted in 15 consecutive contractions for each muscle. Half of the participants began to perform the contractions firstly in the epicondyles muscles of one side of the body, chosen randomly, and the other half

participants began to perform contractions in firstly in the quadriceps muscle of one side of the body.

Data Acquisition and Analysis

Electromyographic (EMG) activity of the muscles was recorded using a sampling rate of 1000 Hz and a frequency band filter of 30-500 Hz. Data were integrated, rectified and segmented off-line into epochs extending from 500 ms prior (baseline) to signal indicating participants moving until 8000 ms later using a Matlab script realized in our laboratory. We considered that participants started to contraction the muscle when EMG signal was at least two standard deviations above background noise levels in base line. These EMG onset were selected as initial time to study motor evoked potentials (MEP) in pre-contraction, contraction and postcontraction. Moreover, mean latency was calculated as the difference between visual and auditory stimulus indicating that participant should to move a part of body and the beginning of the contraction (EMG onset). The time of contraction was calculated for each body location of the EMG signal as the difference between EMG onset and EMG offset. Finally, intensity was calculated as mean of EMG amplitude a long of time contraction.

Electrical brain activity was registered with a 64-channel EEG amplifier. Electrodes were placed following the international 10/20 system and referenced to Cz. Vertical electrooculograms (EOG) were recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 10 kOhm. The sampling rate was 1000 Hz. Filter bandpass was set at 0.1-40Hz.

For the analysis of MEP and corticomuscular coherence, a common baseline was calculated between -1500/-1000 ms. before of EMG onset and EEG signal was segmented in three epochs: pre-contraction (-1000 ms. to EMG onset), contraction (EMG onset to mean EMG offset; 2500 ms.) and post-contraction (mean time of EMG offset to 3000 ms.).

Analysis of the mean amplitude of the MEP area over the central and parietal electrodes in the different epochs was performed. Moreover, to study synchronization between cortical activity and muscular activity, corticomuscular coherence (EEG/EMG) was also calculated over the same electrodes for each body location and epochs for alpha and beta frequency bands (Alpha 8-12.99 Hz., Beta 15-29.99 Hz.).

Statistical analysis

To assess the statistical effects on EMG measures, multivariate analyses of variance for repeated measures with between-subject factors PATIENT GROUP (CP vs. healthy) as well as within-subject factors BODY LOCATION (lateral epicondyles vs. quadriceps) and STIMULATION SIDE (left vs. right) were computed. Corticomuscular coherence and MEP amplitudes over central and parietal electrodes (F3, F4, C3, C4, P3, P4) were analyzed by using multivariate analyses of variance for repeated measures with the between-subject factors PATIENT GROUP (CP vs. healthy) and TIME (pre-contraction vs. contraction) and the additional within-subjects factors BRAIN HEMISPHERE (contralateral vs. ipsilateral to stimulated body side) and LOCATION (frontal vs. central vs. parietal). In all cases, interaction effects were assessed using post-hoc comparisons tests provided by the MANOVA in SPSS (version 15).

RESULTS

Characteristics of muscular contraction

Time and intensity aspects of the muscular contraction in each muscular location were compared between the control group and the group of individuals with CP. Figure 1 displays the EMG curves of two representative subjects from each group (healthy controls vs. CP) for each body location (right lateral epicondyles, left lateral epicondyles, right quadriceps and left quadriceps).

Time contraction was found to be higher in the group of individuals with CP for body location (Main effect GRP, $F_{(1,26)}=14.399$ in lateral epicondyles and $F_{(1,28)}=25.192$ in quadriceps, both $ps<.001$). Significant differences in the latency were found between the groups only for the lateral epicondyles ($F_{(1.26)}=7.976$; $p<.01$), with higher latencies for the group of CP. No significant differences between the groups were found in EMG intensity.

Brain activity elicited by muscular contraction

MEP area amplitude

Motor evoked potentials (MEPs) were analyzed for each location, in pre-contraction, contraction and post-contraction, over central (C3, C4) and parietal electrodes (P3, P4). Muscular evoked potentials (MEPs) elicited by the contraction of lateral epicondyles and quadriceps in these electrodes over the contralateral and ipsilateral hemispheres are shown in Figure 2.

A significant two-way interaction effect GRP*TIME was found for the left quadriceps in both central and parietal electrodes ($F(1,23)=6.891$ and $F(1,24)=3.856$; both $ps<.05$) indicating a enhanced MEP activity of CP in the pre-contraction interval. Also, healthy controls group showed an increasing of MEP amplitudes between pre-stimulus interval and the contraction interval ($p<.05$), whereas no significant change of amplitudes was found in the CP group for the central electrodes during left quadriceps contraction task.

Corticomuscular coherence

Maximum scores of corticomuscular coherence in pre-contraction, contraction and post-contraction were analyzed for each body location over C3, C4, P3 and P4. Figure 3 displays the corticomuscular coherence in lateral epicondyles and quadriceps for each group (CP vs. healthy controls) in the alpha and beta frequency.

In the *alpha band*, a significant GROUP x TIME interaction effect over central electrodes (C3/C4) and parietal electrodes (P3/P4) was observed for right quadriceps (central $F(1,22)=5.060$ parietal $F(1,22)=5.462$ respectively; both $ps<.05$) indicating higher levels of corticomuscular coherence for the control group in the pre-contraction interval ($p<.05$). The comparison in the parietal area also indicated that healthy controls decreased significantly their cortimuscular coherence between the interval pre and post-contraction ($p<.05$), whereas CP levels of coherence did not show any significant differences in any of the time intervals of the spectrum. In the parietal electrodes of right lateral epicondyles, a three-way interaction effect HEMISPHERE x GROUP x TIME was observed ($F(1,16)=3.948$; $p<.05$), showing that the muscular contraction elicited differential brain activation over the hemispheres depending on the group and the time interval. Post-hoc comparisons indicated that healthy controls decreased significantly their cortico-muscular coherence between the interval pre and post-contraction ($p<.05$) in the contralateral hemisphere of the contraction side, whereas this difference was not found in the PC group.

In the *beta band*, we observed a significant GROUP x TIME interaction effect over central electrodes (C3/C4) and parietal electrodes (P3/P4) in left lateral epicondyles (central $F(1,16)=8.129$, parietal $F(1,16)=4.076$ respectively; both $ps<.05$) and right quadriceps (central $F(1,22)=3.501$ and parietal $F(1,22)=4.406$ respectively; both $ps<.05$). In left lateral epicondyles, this interaction indicated higher corticomuscular coherence in the post-contraction time interval compared with the

contraction time interval in the CP group (p<.01), whereas no differences were found for the healthy controls. In right quadriceps, the interaction showed a significant difference between the groups (healthy controls vs. CP) in the pre-contraction interval, indicating higher levels of corticomuscular coherence in the control group (ps<.05). A main effect GROUP was found in the right lateral epicondyles for the parietal electrodes (F(1,16)=6.322; p<.05), showing a higher corticomuscular coherence in the CP group in the contraction and post-contraction intervals (both ps<.05).

DISCUSSION

The aim of this study was to investigate the peripheral and brain process associated to voluntary movements in adults with CP as compared with healthy adults. Specifically we wanted to explore the central motor programming and execution of the muscular contraction in healthy adults compared with bilateral CP adults, analyzing the characteristics of MEP and corticomuscular coherence, as long as the characteristics of their muscular contraction. Our results pointed out that the latency and duration of the muscular response are increased in subjects with CP. It also seems that CP subjects present most of their problems in the planification and relaxation intervals of the motor response. In this sense, we found that the amplitude of muscular evoked-potentials (MEPs) was enhanced in left quadriceps of CP, mainly during the pre-contraction time interval. Nevertheless, the corticomuscular coherence analysis showed significantly higher coherence power in the pre-contraction time interval for the healthy controls. Moreover, healthy controls showed a decrease of corticomuscular coherence between the pre and post-contraction time, while an increase between the contraction and post-contraction time intervals was observed in CP.

Considering the muscular activity, the increased reaction time and duration of the muscular contraction that we found in the CP group agrees with previous studies that showed longer movement durations and slower movement speed in hemiparetic children with CP (Jaspers et al., 2009, Downing et al., 2009, Coluccini et al., 2007, Steenbergen et al., 1998) These increased parameters also may be related with the slowness in motor dexterity shown by population with CP (Gordon & Duff, 1999). On other hand, we did not find significant differences between EMG intensity of healthy controls and subjects with CP. This contrastes with previous research which commonly reported reduced EMG amplitudes during voluntary contraction in individuals with CP (Downing et al., 2009; Rose & McGill, 2005; Elder et al., 2003).

It is widely known that early injuries on the brain may alter the organization of the primary motor cortex (Strata et al. 2004) and impaired central co-ordination of motor activity in individuals with CP have been reported in previous studies (Mockford&Caulton, 2010; Feltham et al., 2010; Hoon et al., 2009; Lauer et al., 2008; Kulak et al., 2006). Our results are in line with these previous studies, showing significant differences between individuals with CP and healthy controls both in central motor programming and execution. Our findings situated the differences between CP subjects and healthy controls mostly on two time intervals: the post-contraction time, when muscle relaxation would take place and the pre-contraction time, suggesting a deficit in the planning, programming and execution of muscular contraction. The deficits in the central organization on the post-contraction time in PC subjects found in our results may be connected with the prolonged duration of EMG activity. These results are similar to previous studies performed with kinematic data, which reported the elongation of the muscular relaxation period in children and adolescents with CP (Downing et al., 2009; Tammik et al., 2008). On the other hand, impairments in CP's anticipatory motor control are in agreement with other authors' reports, who have reported deficitary planning of hand movements in children with hemiplejic CP (Steenbergen et al., 2007; Steenbergen & Gordon, 2006; Mutsaarts et al., 2006, 2005; Gordon & Duff, 1999; Eliasson et al., 1992, 1991).

Our study showed significantly enhanced MEPs amplitudes in CP subjects the pre-contraction interval that lasted up to the contraction execution. MEPs amplitude has been used to measure impairments of neuromuscular activation in other pathologies, as hereditary spastic paraparesis or stroke (Sartucci et al., 2007; Di Lazzaro et al., 2010). Our results agree with the findings of Feltham et al. (2010), who also found higher intensities of mean neuromuscular activity in the arm muscles of hemiparetic children with CP.

Our results of corticomuscular coherence in the control group showed similar patterns as studies performed in healthy population from other authors (Boonstra et al., 2009). Altought no studies of corticomuscular coherence have been found in CP individuals, corticomuscular coherence has been found to be altered in other pathologies such as essential and neurophatic tremor and stroke (Muthuraman et al., 2010; Weiss et al., 2010; Fang et al., 2009). Analyzing corticomuscular and EMG syncronization using time-resolved coherence analysis, allows for a comparison in frequency content and modulation in time (Boonstra et al., 2009). In the human cerebral cortex, oscillations

within band beta and mu have shown to be modulated during and following the preparation and performance of voluntary movement. Before movement initiation, a reduction in oscillatory power in the beta band has been observed over the contralateral sensoriomotor areas in healthy persons. This phenomenon has been associated with neural activation related to movement preparation and execution (Reyns et al., 2008). The study or corticomuscular coherence allowed us to investigate the deficits showed by the CP group in M1, considered the primary generator of this parameter. Our study displays decreased corticomuscular coherence in individuals with CP in both frequency bands, alpha and beta, suggesting that different coupling mechanisms operate in different frequency bands. The alpha band is mediated by the direct corticospinal pathway, while beta band has been related to the descending control from M1 to the motoneurones in the spinal cord (Mima et al., 2000). As beta activity is supresed pior to voluntary movements, the decreased corticomuscular coherence in the beta band showed by PC subjects before the contraction may indicate a lack of active inhibition of the motor network in persons with CP.

Our parallel findings both in central and parietal electrodes in MEPs and corticomuscular coherence are in line with the idea of patterns of increased corticocortical coupling within parietal, premotor and motor network during preparation and execution of praxis movements (Wheaton et al., 2005). Additionally, the scarce hemispheric differences we have found between the motor organization of healthy controls and PC were restricted to the contralateral hemisphere to the motor action body location. Evidence of reorganization of central motor pathways in hemiparetic individuals with CP demonstrated novel ipsilateral motor pathways from the undamaged motor cortex, which implied either an ipsilateral or bilateral projection to the hemiplegic hand, but not from the damaged motor cortex (Krägeloh-Mann & Cans, 2009; Thickbroom et al., 2001). Being our CP sample bilaterally affected, these ipsilateral novel connexions effect may be minor. This result agrees with other studies that found no significant differences in interhemispheric coherence over the central and parietal electrodes in any of the frequency bands in chidren with spastic diplegia (Koeda & Takeshita, 1998).

Our study has some limitations which should be taken into account for the interpretation of the results. First, although our sample of persons with CP seems to be representative of the large population in our community, the sample size was small and the type of cerebral palsy was heterogeneous. Motor evoked potentials and

coritcomuscular coherence provide information from the cortical grey matter, thus the influence of subcortical structures, such as cerebellum or basal ganglia, in motor processing remains underexplored. Nonetheless, our study have offered some novel approximations in the study of motor processing of the CP population, such as the introduction of corticomuscular coherence in the study of motor impairments, and its results may contribute to future approaches in this area.

In conclusion, our results highlight the existence of deficits in motor central processing of persons with CP, mainly in the period prior to the muscular contraction. Nevertheless, studies with ballet dancers and weigh-lifters indicated that oscillatory interaction between the sensorimotor cortex and spinal motoneurones can be changed by long-term specialized use of the muscles and that this neural adaptation may lead to finer control of muscle force (Ushiyama et al., 2010). We are only beginning to understand brain plasticity in persons with CP and the effects of the rehabilitation programs in the reorganization of the developing brain after injury. Our results support the idea that electrophysiological parameters, such as MEPs and corticomuscular coherence, may be useful tools not only for study brain impairments and plasticity after early lesions, but also to measure rehabilitation efficacy in persons with CP.

Acknowledgements

REFERENCES

Boonstra TW, van Wijk BC, Praamstra P, Daffertshofer A. Corticomuscular and bilateral EMG coherence reflect distinct aspects of neural synchronization. Neurosci Lett. 2009;463(1):17-21.

Briellmann RS, Abbott DF, Caflisch U, Archer JS, Jackson GD. Brain reorganisation in cerebral palsy: a high-field functional MRI study. Neuropediatrics. 2002;33(3):162-5.

Burton H, Dixit S, Litkowski P, Wingert JR. Functional connectivity for somatosensory and motor cortex in spastic diplegia. Somatosens Mot Res. 2009;26(4):90-104

Coluccini M, Maini ES, Martelloni C, Sgandurra G, Cioni G. Kinematic characterization of functional reach to grasp in normal and in motor disabled children. Gait Posture. 2007;25(4):493-501.

Di Lazzaro V, Profice P, Pilato F, Capone F, Ranieri F, Pasqualetti P, Colosimo C, Pravatà E, Cianfoni A, Dileone M. Motor cortex plasticity predicts recovery in acute stroke. Cereb Cortex. 2010;20(7):1523-8.

Downing AL, Ganley KJ, Fay DR, Abbas JJ. Temporal characteristics of lower extremity moment generation in children with cerebral palsy. Muscle Nerve. 2009;39(6):800-9.

Elder GC, Kirk J, Stewart G, Cook K, Weir D, Marshall A, Leahey L. Contributing factors to muscle weakness in children with cerebral palsy. Dev Med Child Neurol. 2003;45(8):542-50.

Eliasson AC, Gordon AM, Forssberg H. Basic co-ordination of manipulative forces of children with cerebral palsy. Dev Med Child Neurol. 1991;33(8):661-70.

Eliasson AC, Gordon AM, Forssberg H. Impaired anticipatory control of isometric forces during grasping by children with cerebral palsy. Dev Med Child Neurol. 1992;34(3):216-25.

Fang Y, Daly JJ, Sun J, Hvorat K, Fredrickson E, Pundik S, Sahgal V, Yue GH. Functional corticomuscular connection during reaching is weakened following stroke. Clin Neurophysiol. 2009;120(5):994-1002.

Feltham MG, Ledebt A, Deconinck FJ, Savelsbergh GJ. Assessment of neuromuscular activation of the upper limbs in children with spastic hemiparetic cerebral palsy during a dynamical task. J Electromyogr Kinesiol. 2010;20(3):448-56.

Gordon AM, Duff SV. Fingertip forces during object manipulation in children with hemiplegic cerebral palsy. I: anticipatory scaling. Dev Med Child Neurol. 1999;41(3):166-75.

Hoon AH Jr, Stashinko EE, Nagae LM, Lin DD, Keller J, Bastian A, Campbell ML, Levey E, Mori S, Johnston MV. Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Dev Med Child Neurol. 2009;51(9):697-704.

Jaspers E, Desloovere K, Bruyninckx H, Molenaers G, Klingels K, Feys H. Review of quantitative measurements of upper limb movements in hemiplegic cerebral palsy. Gait Posture. 2009;30(4):395-404.

Koeda T, Takeshita K. Electroencephalographic coherence abnormalities in preterm diplegia. Pediatr Neurol. 1998;18(1):51-6.

Krägeloh-Mann I, Cans C. Cerebral palsy update. Brain Dev. 2009;31(7):537-44.

Kułak W, Sobaniec W, Boćkowski L. EEG spectral analysis and coherence in children with hemiparetic cerebral palsy. Med Sci Monit. 2005;11(9):CR449-55.

Kułak W, Sobaniec W, Kuzia JS, Boćkowski L. Neurophysiologic and neuroimaging studies of brain plasticity in children with spastic cerebral palsy. Exp Neurol. 2006;198(1):4-11.

Lauer RT, Johnston TE, Smith BT, Lee SC. Lower extremity muscle activity during cycling in adolescents with and without cerebral palsy. Clin Biomech. 2008;23(4):442-9.

Maegaki Y, Maeoka Y, Ishii S, Eda I, Ohtagaki A, Kitahara T, Suzuki N, Yoshino K, Ieshima A, Koeda T, Takeshita K. Central motor reorganization in cerebral palsy patients with bilateral cerebral lesions. Pediatr Res. 1999;45(4 Pt 1):559-67.

Meng F, Tong KY, Chan ST, Wong WW, Lui KH, Tang KW, Gao X, Gao S. Cerebral plasticity after subcortical stroke as revealed by cortico-muscular coherence. IEEE Trans Neural Syst Rehabil Eng. 2009;17(3):234-43.

Mima T, Hallett M. Corticomuscular coherence: a review. J Clin Neurophysiol. 1999;16(6):501-11.

Mockford M, Caulton JM. The pathophysiological basis of weakness in children with cerebral palsy. Pediatr Phys Ther. 2010;22(2):222-33.

Muthuraman M, Heute U, Deuschl G, Raethjen J. The central oscillatory network of essential tremor. Conf Proc IEEE Eng Med Biol Soc. 2010;1:154-7.

Mutsaarts M, Steenbergen B, Bekkering H. Anticipatory planning deficits and task context effects in hemiparetic cerebral palsy. Exp Brain Res. 2006;172(2):151-62.

Mutsaarts M, Steenbergen B, Bekkering H. Anticipatory planning of movement sequences in hemiparetic cerebral palsy. Motor Control. 2005;9(4):439-58.

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39(4): 214-23.

Pelosi L, Lanzillo B, Perretti A, Santoro L, Blumhardt L, Caruso G. Motor and somatosensory evoked potentials in hereditary spastic paraplegia. J Neurol Neurosurg Psychiatry. 1991;54(12):1099-102.

Platz T, Kim IH, Pintschovius H, Winter T, Kieselbach A, Villringer K, Kurth R, Mauritz KH. Multimodal EEG analysis in man suggests impairment-specific changes in movement-related electric brain activity after stroke. Brain. 2000;123 Pt 12:2475-90.

Reyns N, Houdayer E, Bourriez JL, Blond S, Derambure P. Post-movement beta synchronization in subjects presenting with sensory deafferentation. Clin Neurophysiol. 2008;119(6):1335-45.

Rose J, McGill KC. Neuromuscular activation and motor-unit firing characteristics in cerebral palsy.Dev Med Child Neurol. 2005;47(5):329-36.

Sartucci F, Tovani S, Murri L, Sagliocco L. Motor and somatosensory evoked potentials in Autosomal Dominant Hereditary Spastic Paraparesis (ADHSP) linked to chromosome 2p, SPG4. Brain Res Bull. 2007;74(4):243-9.

Steenbergen B, Gordon AM. Activity limitation in hemiplegic cerebral palsy: evidence for disorders in motor planning. Dev Med Child Neurol. 2006;48(9):780-3.

Steenbergen B, Hulstijn W, Lemmens IH, Meulenbroek RG. The timing of prehensile movements in subjects with cerebral palsy. Dev Med Child Neurol. 1998;40(2):108-14.

Steenbergen B, Verrel J, Gordon AM. Motor planning in congenital hemiplegia. Disabil Rehabil. 2007;29(1):13-23.

Strata F, Coq JO, Byl N, Merzenich MM. Effects of sensorimotor restriction and anoxia on gait and motor cortex organization: implications for a rodent model of cerebral palsy. Neuroscience. 2004;129(1):141-56.

Tammik K, Matlep M, Ereline J, Gapeyeva H, Pääsuke M. Quadriceps femoris muscle voluntary force and relaxation capacity in children with spastic diplegic cerebral palsy. Pediatr Exerc Sci. 2008;20(1):18-28.

Thickbroom GW, Byrnes ML, Archer SA, Nagarajan L, Mastaglia FL. Differences in sensory and motor cortical organization following brain injury early in life. Ann Neurol. 2001;49(3):320-7.

Ushiyama J, Takahashi Y, Ushiba J. Muscle dependency of corticomuscular coherence in upper and lower limb muscles and training-related alterations in ballet dancers and weightlifters.J Appl Physiol. 2010;109(4):1086-95.

Weiss D, Govindan RB, Rilk A, Wächter T, Breit S, Zizlsperger L, Haarmeier T, Plewnia C, Krüger R, Gharabaghi A. Central oscillators in a patient with neuropathic tremor: Evidence from intraoperative local field potential recordings. Mov Disord. 2011;26(2):323-7.

Wheaton LA, Nolte G, Bohlhalter S, Fridman E, Hallett M. Synchronization of parietal and premotor areas during preparation and execution of praxis hand movements.Clin Neurophysiol. 2005;116(6):1382-90.

Wittenberg GF. Motor mapping in cerebral palsy.Dev Med Child Neurol. 2009;51 Suppl 4:134-9.

FIGURE LEGENDS

Table I. Clinical characteristics of individuals with cerebral palsy. (M=male, F=female, BS=bilateral spastic, D=dyskinetic, A=ataxic).

Figure 1. EMG curves of two representative subjects from each group (healthy controls vs. CP) for each body location (right lateral epicondyles, left lateral epicondyles, right quadriceps and left quadriceps).

Figure 2. Comparative graphics of latency and duration of muscular contraction between healthy controls and CP for each body location (right lateral epicondyles, left lateral epicondyles, right quadriceps and left quadriceps).

Figure 3. Muscular evoked potentials (MEPs) elicited by the contraction of lateral epicondyles and quadriceps in the central and parietal electrodes over the contralateral hemisphere for healthy controls and individuals with CP.

Figure 4. Corticomuscular coherence in lateral epicondyles and quadriceps for each participant group (cerebral palsy vs. healthy controls) in the alpha and beta frequency bands, separated by body locations (right vs. left) and electrodes (C3, C4, P3 and P4).

Table I

ID	Sex	Age	CP subgroup	Gestational age(weeks)	GMFCS	Mental retardation	Epilepsia	Medication
1	F	12	BS	36	2	No	Yes	Antiepileptic
2	F	12	A	40	4	No	No	No
3	M	12	BS	31	3	Mild	No	Antidepressive
4	M	21	A	40	1	Moderate	No	No
5	M	26	BS	40	1	Moderate	No	No
6	M	27	BS	40	1	Moderate	No	No
7	M	27	BS	40	3	Moderate	No	No
8	M	28	BS	40	1	Severe	No	Antidepressive
9	M	28	A	40	2	Severe	Yes	No
10	M	30	BS	30	3	No	Yes	No
11	F	35	BS	40	2	Severe	Yes	Antiepileptic
12	M	38	A	40	2	Mild	Yes	Antiepileptic
13	F	52	BS	40	4	No	Yes	Antiepileptic
14	M	54	D	32	1	Mild	NO	Muscular relaxant

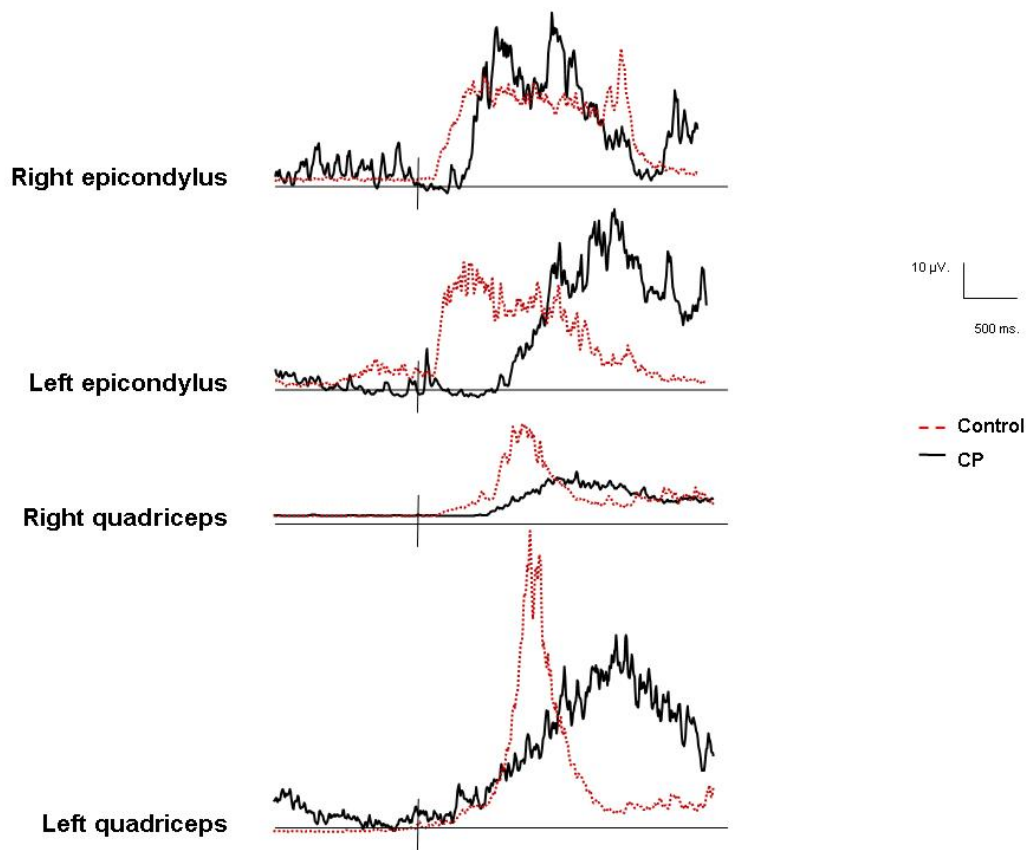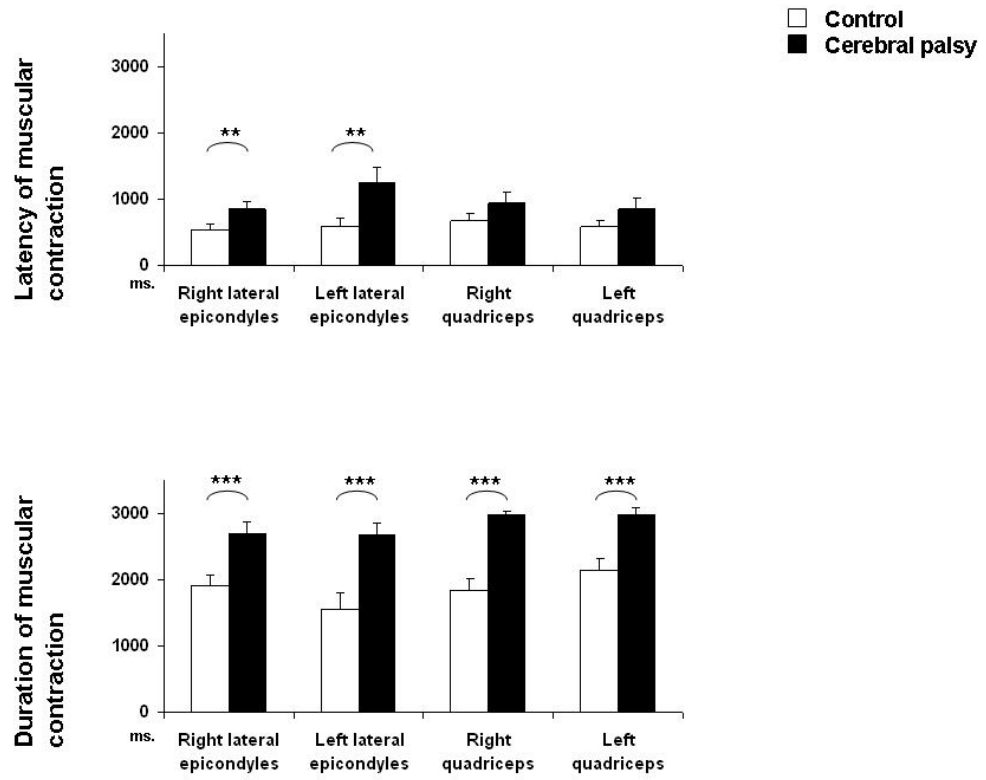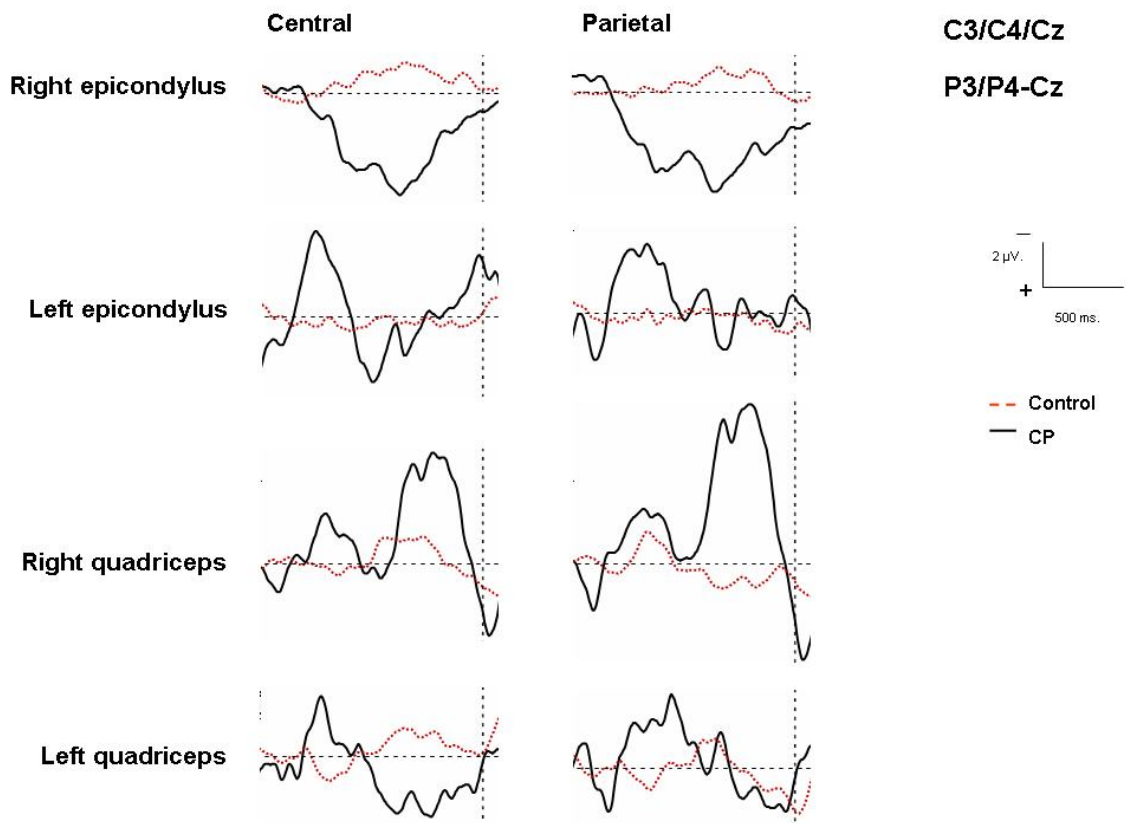# Figure 1

Figure 2

Figure 3

Figure 4

A)

C3/C4-Cz

B)

P3/P4-Cz

Right lateral epicondyle   Left lateral epicondyle

Control

Cerebral
palsy

Right quadriceps   Left quadriceps

Control

Cerebral
palsy

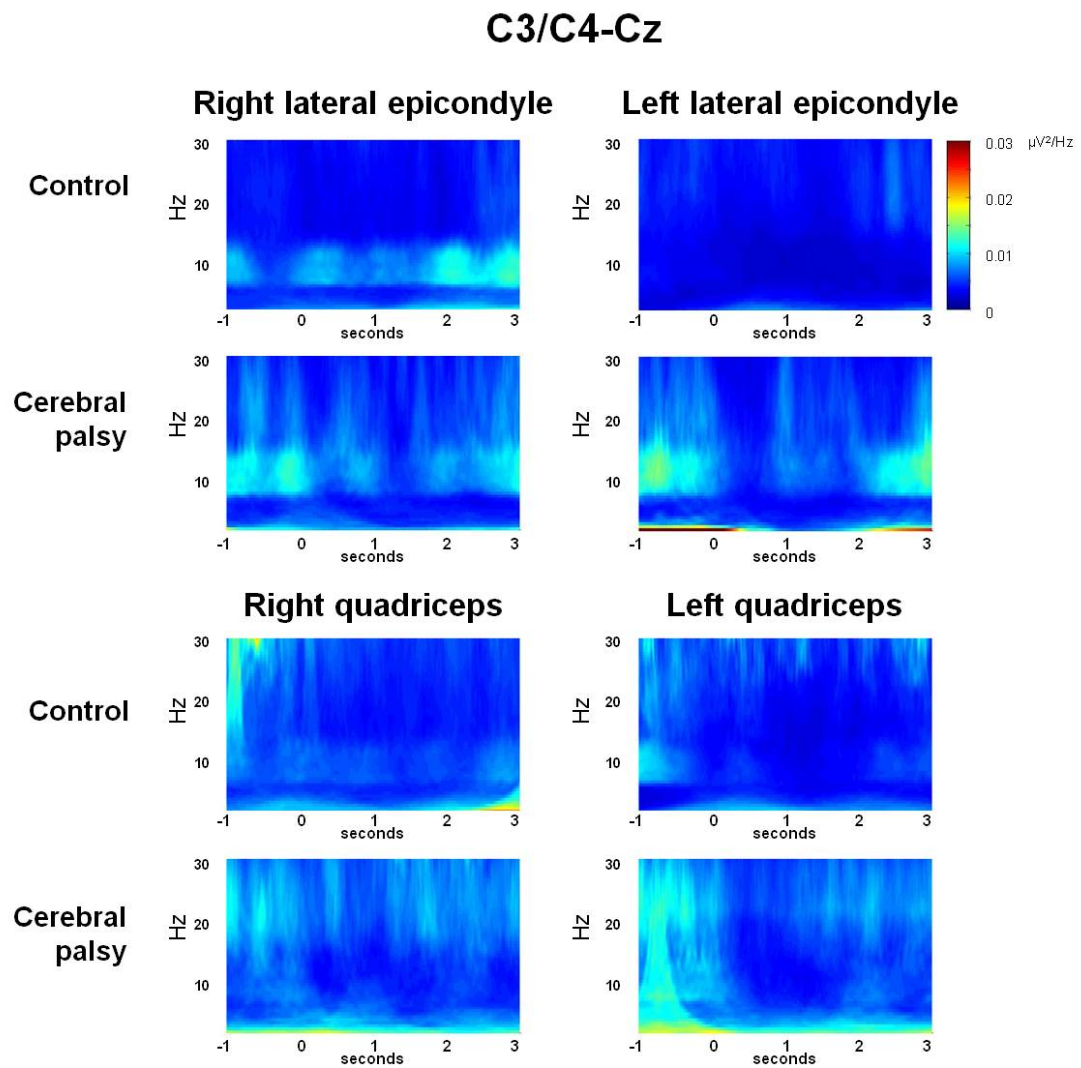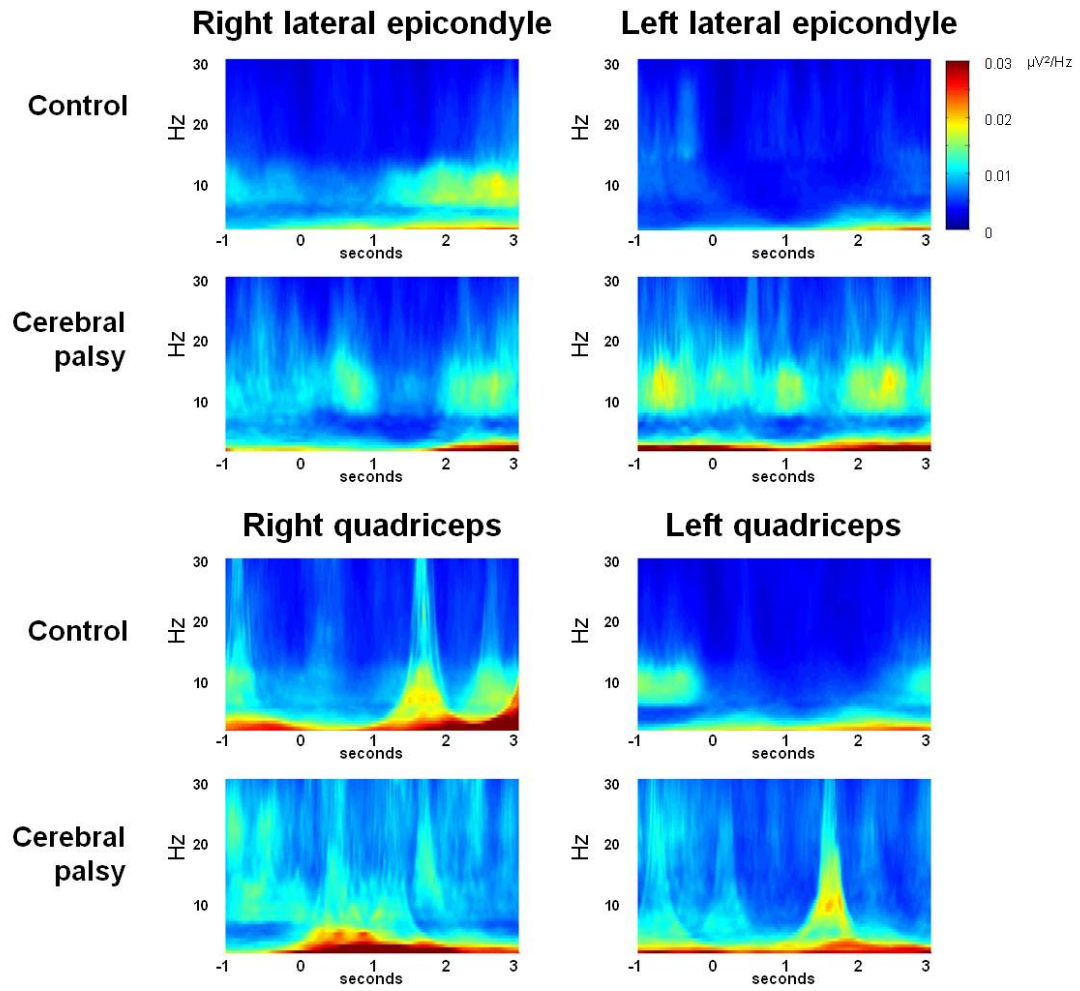*Experimento 4. Eficacia de un programa de intervención somatosensorial en los déficits somestésicos, nociceptivos y motores de personas con parálisis cerebral*

Presentación de la investigación

Los datos neurofisiológicos de los experimentos anteriores nos hicieron plantearnos la necesidad de explorar la aplicabilidad clínica de estos resultados y de los programas de intervención clínica que proponíamos en nuestras conclusiones. Para ello, nos propusimos comprobar si la mera estimulación somatosensorial y propioceptiva, sin ningún tipo de intervención motora específica, produciría cambios en la sensibilidad somestésica, dolorosa y en la actividad motora de personas con parálisis cerebral. De este modo, comenzamos a aplicar un programa de terapia somatosensorial a personas adultas con parálisis cerebral, de forma paralela a sus sesiones de terapia habituales. Se realizaron una evaluación previa al inicio del tratamiento y dos evaluaciones posteriores al tratamiento, una 1 semana después de la finalización y otra 3 meses después. En ellas se evaluó la motricidad fina, intensidad dolorosa, propiocepción, umbrales de sensibilidad táctil, umbrales de sensibilidad dolorosa a la presión, esterognosia y diferenciación de texturas de las partes del cuerpo sometidas a tratamiento (manos, cara y boca). Curiosamente, el tratamiento se mostró más efectivo en el aumento de los umbrales de dolor a la presión, efecto que se mantenía 3 meses después del cese de la terapia. La eficacia de la intervención somatosensorial en la reducción de la sensibilidad dolorosa, junto con los descubrimientos previos referidos a la pobre sensibilidad táctil de las personas con parálisis cerebral, apoya la teoría de que la escasez de experiencias táctiles que tienen estas personas puede determinar una sensibilización para los estímulos dolorosos. Este descubrimiento es de suma relevancia y obliga a considerar la necesidad de implementar una terapia somatosensorial desde edades tempranas. A continuación, se adjunta un manuscrito que detalla la metodología y los resultados obtenidos mediante este programa de intervención.

Manuscrito:

Efficacy of a somatosensory therapy program in the reduction of pain threshold in adults with cerebral palsy

EFFICACY OF A SOMATOSENSORY THERAPY PROGRAM IN THE REDUCTION OF PAIN THRESHOLD IN ADULTS WITH CEREBRAL PALSY

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Running title: Somatosensory therapy, pain and cerebral palsy.

Abstract

Objective. Somatosensory deficits are a serious problem for people with cerebral palsy. Proprioception, tactile processing, sterognosis and pain have been shown to be impaired in this population. However, little is known about the efficacy of interventions addressed to improve somatosensory parameters. ***Methods.*** A group of adults with cerebral palsy participate in the study. Seventeen participants received somatosensory therapy in face and hands. Assessments of tactile sensitivity, pain and fine motor performance were carried out once before the intervention (pretest) and at 1 week and 3 months after the intervention (posttests). ***Results.*** Participants from the intervention group showed significant enhancement of their pain thresholds in all the areas, significant enhancement sterognosis of left hand and significant reduced touch sensitivity thresholds in left cheek, left thumb, right thenar eminence and both hand backs between the pretest and posttest. Differences in pain thresholds were maintained three months after the end of the intervention. No improvement was found in texture discrimination, propioception, VAS scores or fine motor performance. ***Conclusions.*** Data suggest the possibility that somatosensory therapy modifies the perception of pain in adults with cerebral palsy. The lack of tactile experiences may be the key factor which causes the enhanced sensibility to pain in people with cerebral palsy. This hypothesis may have implications for future neuromodulatory treatment of pain complaints in children and adults with cerebral palsy.

Keywords: somatosensory therapy, cerebral palsy, sensitivity, pain

INTRODUCTION

In the complex context of impairments that characterize individuals with cerebral palsy (CP), it has been a growing recognition that somatosensory deficits may have a capital importance. Thus, it has been shown to that persons with CP have poorer tactile discrimination, stereognosis and proprioception than healthy population (Wingert et al., 2009; Sanger and Kukke, 2007; McLaughlin et al., 2005) as well as increased levels of pain (Malone & Vogtle, 2010; Doralp & Bartlett, 2010; Parkinson et al., 2010; Vogtle LK., 2009). It is well-known the relationship between the deficit of somatosensorial processing and the motor impairment (Kinnucan et al., 2010; Bumin & Kavak, 2008; Gordon et al., 2006) but it is also being suggested the relationship between the poor tactile sensitivity and higher pain perception in persons with CP, due to long-term changes in the processing of the somatosensory afferences caused by the abnormal repetitive perception from early ages (Schmelzle-Lubiecki et al., 2007).

Considering the close relationship between somatosensory deficits and motor performance and pain, it seems plausible that a somatosensory therapy program may improve these functions in persons with CP. Previous work has shown that training and learning can induce powerful changes in the organization of the primary somatosensory cortex (Schaefer M. et al, 2005) and some studies have proven the benefits of this therapy in other pathologies, such as spinal cord injury and stroke (Hoffman & Field-Fote, 2010; Hillier & Dunsford, 2006). Nevertheless, studies which report the results of this intervention in persons with CP are scarce and contradictory (Kerem et al., 2001; Bumin & Kayihan, 2001; Semenova 1997; Hylton & Allen, 1997).

In the present study, we conducted a pilot trial of 12 weeks duration to evaluate the effects of somatosensory therapy in adults with CP. In particular, we measured the effects of a somatosensory intervention in tactile sensitivity, stereognosis, propioception, pain and fine motor function. Pain and decreased participation in physical therapy programs are influent factors in the loss of functionality and daily performance over time in the adult population with CP (Murphy et al., 2010). Therefore, the results obtained in the adult population with CP may allow to identificate the most adequate intervention, and thus, to prevent some of the long-term problems from early ages.

METHODS

Participants

Subjects with cerebral palsy (CP) were recruited from occupational centers established in the island of Majorca (Spain) between January and July of 2010. Potential subjects were initially identified by their own physicians and invited to participate using an informational letter explaining the details of the research study. Inclusion criteria were: (1) age older than 18 years, and (2) cognitive level that allows understanding and participating in the activities of the intervention program. Augmentative communication devices and information from parents and caregivers were used as needed to facilitate data collection in subjects with communication difficulties.

Twenty adults with CP met the inclusion criteria and decided to participate in the study. The participants receive somatosensory therapy in addition to the physiotherapy program offered by their centre. Two of the 20 participants included in the intervention program, withdrew during the intervention because the study required too much commitment; another subject was lost to follow-up because of failure to attend the posttest evaluation. Finally, 17 subjects were included in the intervention program (5 females, mean age 30y, 5 months). Subjects or their parents reported their age and sex. Type of cerebral palsy and cognitive level were obtained from the health history. Level of gross motor impairment was determined using the Gross Motor Function Classification Scale (GMFCS) (Palisano et al., 1997) and level of fine motor impairment was determined using the Manual Ability Classification System (MACS) (Eliasson et al., 2006). Table 1 displays clinical characteristics of participants with cerebral palsy within each group.

– Please, insert Table 1 about here –

All participants granted written informed consent according with the Declaration of Helsinki. Parents or legal tutors signed informed consents and participants corroborated their decisions to participate in the study. The study was approved by the Ethics Committee of the Regional Government of the Balearic Islands.

Somatosensory therapy procedure

The intervention program consisted on 24 sessions of 45 minutes during 12 weeks. All participants continued to receive physiotherapy according to the program established at

their centre. The standard physiotherapy program offered by the centre was individualized according to the needs of each person and comprised one to two therapeutic sessions per week. In addition, the participants received somatosensory therapy in two sessions per week at the participants' centre. The treatment was administered in group sessions by two fully trained physical therapists. The reliability of a group intervention has been established previously in the literature (Bumin & Kayihan, 2001).

The physical therapists documented the activities used for each treatment session as well as other clinical observations made during the therapy sessions. A list of 61 tasks across 4 categories was established for the somatosensory therapy program. These tasks included tactile tasks (eg., touching different textures, tactile location), proprioception tasks (eg., pushing and weight exercises), vibration stimulation and stereognosis, (eg., object recognition). The therapy was planned involving all the impaired body locations (face, mouth and hands). The week program planning also assured that the grade of difficulty of the activities would increase from the first to the second session of the week. None of the measures or objects that were used in the pretest and posttests was used in the therapy sessions. An example of the typical development of sessions in one week can be seen in Table 2.

– Please, insert Table 2 about here –

Somatosensory testing

Outcome measures were selected for providing information at 3 levels: tactile sensitivity, pain sensitivity and motor performance.

Each participant was evaluated once before the intervention (pretest) and two times after the intervention, one immediately after the end of the intervention and a second time three months after the end of the intervention (posttests). All of the evaluations took place in the occupational centre attended by each participant. The same evaluator, member of the research team (IR), performed all testing of all the subjects. This evaluator was different from the physical therapists who performed the somatosensory therapy program.

All participants in the study were administered following tasks to measure somatosensory skills:

Touch. Fine touch sensitivity using von Frey monofilaments (Keizer et al., 2008) was measured bilaterally at six body locations (lips, cheeks, thenar eminences, thumb fingers, index fingers and the back of the hands). Von Frey monofilaments were composed by a set of plastic filaments of different diameter (0.14-1.01 mm.). The test was performed touching the skin in a perpendicular way, pressing it slowly down until it buckles, holding it steady during 1.5 seconds and removing it in the same way as it was applied. After several trials to assure the understanding of the procedure, subjects were instructed to notify the experimenter if they felt any sensation of touch by saying "yes" or "not". The procedure started with a thick filament and depending on subjects' answers, thicker or thinner filaments were applied. The sensitivity score for each body location was calculated as the mean of the three thinnest filaments detected. Null stimuli were also used to find false positive responses and responses delayed more than 3 seconds were noted as abnormal. Body locations were stimulated in a pseudo-randomized order.

Pressure pain. Pressure pain thresholds (expressed in kgf/cm^2) were measured with a digital dynamometer and using a flat rubber tip ($1 \ cm^2$). Subjects were asked to say 'pain' when the pressure became painful. Pressure was released when either the pain detection threshold had been reached or when the maximum pressure of the algometer (equal to 13.0 kgf) was reached. Pressure stimuli were applied bilaterally in pseudo-randomized order at the same six body locations as before (lips, cheeks, thenar eminences, thumb fingers, index fingers and the back of the hands). Before the assessment, subjects were familiarized with the procedure using non-painful ranges to relieve potential anxiety. The reliability of this procedure for assessing pain sensitivity has been demonstrated in previous studies (Cathcart and Pritchard, 2006).

Intensity of pain. A 11-point visual analogical scale was used to assess intensity of pain. The reliability of this procedure for assessing pain sensitivity has been demonstrated in previous studies (Cathcart and Pritchard, 2006).

Texture recognition. To asses gross sensitivity a task of recognition of opposite textures (soft/hard, smooth/rough) was performed touching bilaterally the cheeks, lips and hands of the participants, who were eyed-blinded. Participants were asked by giving them two options (soft or hard, smooth or rough) to facilitate the answer. The four opposite textures were tested, given 1 point of score per each being recognized. Texture recognition has been used frequently as a way to test sensitivity (Carey & Matyas, 2005).

Stereognosis. To assess stereognosis skills of both hands 10 objects were used (coin, bank note, scissors, pencil, biro pen, comb, towel, sponge, glass and cup). An object inside a bag was placed in one of the hands of the participant, who was eyed-blinded. The participant could move and touch the object with only the hand tested. In participants unable to move their hand, the examiner moved the object in the participant's hands. Stereognosis was scored from 0 to 2 for each object (2=Normal, the object is correctly named or matched, 1=Impaired, attempts to describe the object or some of its features, 0=Absent, the participant is unable to identify the object in any manner) and a total score was calculated with the sum of the ten different scores. This way to assess stereognosis was extracted from the Nottinghan Sensory Assessment, whose reliability has been proven in previous works (Gaubert & Mockett, 2000).

Proprioceptive task. To assess proprioceptive skills, two different tasks were performed with eyes-closed and in all joints of the upper limb: a) recognition of the existence of movement, and b) final position in passive movement of a joint reported verbally or performance of the same movement with the contralateral limb. Each task was repeated five times and the average number of correct trials was used as an index of proprioceptive skills. This procedure has been used successfully in previous studies (Wingert et al., 2009).

Fine motor skills. To assess hand fine motor skills a modification of the Purdue Pegboard test was used. The subject was seated in front of a table where the Purdue Pegboard test was placed. On the board, two cups on the far right and far left corner contained 25 pins in each. Three tests were performed: test for the right hand, test for the left hand and test for both hands. The subject had to pick up one pin at a time with the hand tested (ex. with the right hand from the right-handed cup) and, starting with the top hole, place each pin in the correspondent row (right-hand row in our example). The subject was instructed to place as many pins as possible from the order of "Begin" to the order of "Stop". To test both hands performance, the subject was instructed to pick up a pin from the right-hand cup with the right hand and, at the same time, pick up a pin from the left-hand cup with the left hand and then place the pins down the rows. Each test lasted 30 seconds. The assembly parts of the original test were excluded due to the impaired fine motricity that may have the population with CP. This test has been previously used to assess the fine hand performance in subjects with CP (Arnould et al., 2007).

Statistical analysis

To assess differences before and after the somatosensory therapy program, parametric and non-parametric tests for repeated samples (t-tests for related-samples and Wilconson test for related-samples) were used, depending of the characteristics of the variable.

RESULTS

Participants showed to have low intensity of pain (0-2 in an eleven-point VAS scale) both before and after the intervention in both lips, cheeks and hands. The therapy program did not modified the perception of pain of the subjects.

Participants showed significantly reduced tactile thresholds in left cheek (Z= -2.670, p<.01), right thenar eminence (Z= -2.050, p<.05), left thumb (Z= -2.213, p<.05), back of the right hand (Z=-2.247, p<.05) and back of the left hand (Z= -2.156, p<.05). These differences were maintained only in the back of the left hand after three months of the end of the intervention (Z= -2.004, p<.05). Table 2 displays the mean touch sensitivity in all the examined body locations separated for time of examination (before intervention vs. after intervention vs. three months after the end of the intervention).

-Please, insert Table 3 about here-

Participants from the intervention group showed significantly increased pressure pain thresholds in all the body locations (all ts>-2, all ps<.05). These differences were maintained in all the body locations (all ts>-2, all ps<.05) except in right index (t(16)=-2.104, p=.052), that did not showed significant differences, and left lip (t(16)=5.785, p<.001), that showed a significant decrease of the pain threshold. Table 3 displays the mean pain sensitivity in all the examined body locations separated for time of examination (before intervention vs. after intervention vs. three months after the end of the intervention).

Stereognosis of left hand changed before and after the teraphy program intervention (Z= -2.146, p<.05), whereas no differences were found in sterognosis of right hand before and after the intervention in any of the two groups.

Neither texture recognition (soft/hard, smooth/rough) in face and hand, proprioception of the upper limbs or fine motor task scores showed significant differences before and after the intervention.

DISCUSSION

The objective of this study was to evaluate the efficacy of a somatosensory therapy program in adults with CP. In particular, we measured the effects of a somatosensory intervention in tactile sensitivity, stereognosis, propioception, pain and fine motor function. Our results demonstrate a significant enhancement of pain pressure thresholds of all the tested body locations after the therapy program, enhancement that was maintained 3 months after the end of the intervention in 10 of the 12 body locations. Moreover, fine touch sensitivity thresholds of 5 body locations (left cheek, right thenar eminence, left thumb and both backs of the hands) and sterognosis of left hand improved immediately after the therapy program, but the effect did not remain three months after the end of the intervention.

Our study demonstrates that somatosensory impairments may improve with a therapy directly addressed to these deficits. This fact results relevant because somatosensory impairments are considered important comorbilities in persons with CP (Doralp & Bartlett, 2010; Parkinson et al., 2010; Malone & Vogtle, 2010; Vogtle LK., 2009; Wingert et al., 2009). Curiously, the somatosensory therapy was more effective in the improvement of pain thresholds than in the improvement of other somatosensory parameters. These finding is of particular importance, since pain has been identified as a major health concern in cerebral palsy (Vogtle LK, 2009). Some previous studies have proven that touch hyposensitivity could be linked to increased pain sensitivity in children with early injury (Riquelme & Montoya, 2010; Schmelzle-Lubiecki et al., 2007). These data reinforced the hypothesis that the lack of tactile experiences may be the key factor which causes the enhance sensibility to pain in people with CP.

The abnormal processing of information arising from the body including sterognosis, proprioception, touch sensitivity and pain, are considered to be indicative of abnormal cerebral sensory function (Carlson & Brooks, 2010) and may produce plastic changes in somatosensory cortices. All these findings are basically consistent with results of human and animal studies indicating that early infant injury has not only local, but also global long-term consequences upon sensory processing (Riquelme & Montoya, 2010; Schmelzle-Lubiecki et al., 2007). There have been also some results indicating that activity-dependent plasticity could play a role in the evolution of clinical signs of motor dysfunction in children with CP (Eyre JA., 2007). Thus, the improvement of pain pressure thresholds and its maintenance over the time, suggest the

possibility of a reorganization of the peripheric and central processing of pain sensitivity. Our results are consistent with this possibility and provide initial support for further experiments directed at studying the neurophysiological effects of sensory intervention.

Our data did not show changes in the fine motor function of hands after the somatosensory therapy program. These results contrast with other studies which revealed a significant increase in cortical motor representation muscles after somatosensory transcutaneous electrical nerve stimulation in healthy persons (Meesen et al., 2010). Moreover, it has been proven that the use of pressure splints produced changes on the spasticity and range of movement in children with spastic CP (Kerem et al., 2001). The disagreement with our results may be produced by the age of the subject sample. Changes in the motor performance on adults in such a short period of time and with a non-motor-addressed intervention may be difficult to arise. The remaining of poor propioception scores after the intervention may also have influence on the motor function performance. Other factor to have into account is that the motor performance was tested only with a test of a very fine manipulative task; results might be different with the use of other motor measurements.

Our study has some limitations which should be taken into account for the interpretation of the results. Firstly, the study lacks of a control group to compare the results obtained with our sample. Secondly, although our sample of persons with CP seems to be representative of the population in our community, the sample size was small and the type of cerebral palsy and location of cerebral injury was heterogeneous. Moreover, the results obtained with an adult sample may be different of those that could be obtained with a children sample, due to the higher brain plasticity widely recognized in lower ages. Nevertheless, our study may be useful as a pilot trial study, laying the scientific basis and guiding the selection of appropriate outcome measures for implementation of future randomized designs with bigger samples and in different ages.

All these findings highlight the importance of somatosensory experience in the enhanced sensibility to pain demonstrated in persons with CP (Riquelme & Montoya, 2010). The increase of somatosensory experiences provided by somatosensory therapy may have effects on the pain processing and reduce the perception of pain in the population with CP. This hypothesis may have implications for future neuromodulatory treatment of pain complaints in children and adults with cerebral palsy. Early interventions should address to decrease sensitivity to pain throughout the adult years.

REFERENCES

Arnould C, Penta M, Thonnard JL. Hand impairments and their relationship with manual ability in children with cerebral palsy. J Rehabil Med. 2007;39(9):708-14.

Bumin G, Kavak ST. An investigation of the factors affecting handwriting skill in children with hemiplegic cerebral palsy. Disabil Rehabil. 2010;32(8):692-703.

Bumin G, Kayihan H. Effectiveness of two different sensory-integration programmes for children with spastic diplegic cerebral palsy. Disabil Rehabil. 2001;23(9):394-9.

Carey LM, Matyas TA. Training of somatosensory discrimination after stroke: facilitation of stimulus generalization. Am J Phys Med Rehabil. 2005;84(6):428-42.

Carlson MG, Brooks C. The effect of altered hand position and motor skills on stereognosis. J Hand Surg Am. 2009;34(5):896-9.

Cathcart S, Pritchard D. Reliability of pain threshold measurement in young adults. J Headache Pain. 2006; 7(1): 21-6.

Doralp S, Bartlett DJ. The prevalence, distribution, and effect of pain among adolescents with cerebral palsy. Pediatr Phys Ther. 2010;22(1):26-33.

Eliasson AC, Krumlinde Sundholm L, Rösblad B, Beckung E, Arner M, Öhrvall AM , Rosenbaum P. The Manual Ability Classification System (MACS) for children with cerebral palsy: scale development and evidence of validity and reliability. Dev Med Child Neur. 2006. 48:549-554.

Eyre JA. Corticospinal tract development and its plasticity after perinatal injury. Neurosci Biobehav Rev. 2007;31(8):1136-49.

Gaubert CS, Mockett SP. Inter-rater reliability of the Nottingham method of stereognosis assessment. Clin Rehabil. 2000;14(2):153-9.

Gordon AM, Charles J, Steenbergen B. Fingertip force planning during grasp is disrupted by impaired sensorimotor integration in children with hemiplegic cerebral palsy. Pediatr Res. 2006;60(5):587-91.

Hillier S, Dunsford A. A pilot study of sensory retraining for the hemiparetic foot post-stroke. Int J Rehabil Res. 2006;29(3):237-42.

Hoffman LR, Field-Fote EC Functional and corticomotor changes in individuals with tetraplegia following unimanual or bimanual massed practice training with somatosensory stimulation: a pilot study. J Neurol Phys Ther. 2010;34(4):193-201.

Hylton N, Allen C. The development and use of SPIO Lycra compression bracing in children with neuromotor deficits. Pediatr Rehabil. 1997;1(2):109-16.

Keizer D, Fael D, Wierda JM, van Wijhe M. Quantitative sensory testing with Von Frey monofilaments in patients with allodynia: what are we quantifying? Clin J Pain 2008; 24(5): 463-6.

Kerem M, Livanelioglu A, Topcu M. Effects of Johnstone pressure splints combined with neurodevelopmental therapy on spasticity and cutaneous sensory inputs in spastic cerebral palsy. Dev Med Child Neurol. 2001;43(5):307-13.

Kinnucan E, Van Heest A, Tomhave W. Correlation of motor function and stereognosis impairment in upper limb cerebral palsy. J Hand Surg Am. 2010;35(8):1317-22.

Malone LA, Vogtle LK. Pain and fatigue consistency in adults with cerebral palsy. Disabil Rehabil. 2010;32(5):385-91.

McLaughlin JF, Felix SD, Nowbar S, Ferrel A, Bjornson K, Hays RM. Lower extremity sensory function in children with cerebral palsy. Pediatr Rehabil. 2005;8(1):45-52.

Meesen RL, Cuypers K, Rothwell JC, Swinnen SP, Levin O. The effect of long-term TENS on persistent neuroplastic changes in the human cerebral cortex. Hum Brain Mapp. 2011;32(6):872-82.

Murphy KP. The adult with cerebral palsy. Orthop Clin North Am. 2010;41(4):595-605.

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39(4): 214-23.

Parkinson KN, Gibson L, Dickinson HO, Colver AF. Pain in children with cerebral palsy: a cross-sectional multicentre European study. Acta Paediatr. 2010;99(3):446-51.

Riquelme I, Montoya P. Developmental changes in somatosensory processing in cerebral palsy and healthy individuals. Clin Neurophysiol. 2010;121(8):1314-20.

Sanger TD, Kukke SN. Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. J Child Neurol. 2007;22(3):289-93.

Schaefer M, Flor H, Heinze HJ, Rotte M. Dynamic shifts in the organization of primary somatosensory cortex induced by bimanual spatial coupling of motor activity. Neuroimage. 2005;25(2):395-400.

Schmelzle-Lubiecki BM, Campbell KA, Howard RH, Franck L, Fitzgerald M. Long-term consequences of early infant injury and trauma upon somatosensory processing. Eur J Pain. 2007;11(7):799-809.

Semenova KA. Basis for a method of dynamic proprioceptive correction in the restorative treatment of patients with residual-stage infantile cerebral palsy. Neurosci Behav Physiol. 1997;27(6):639-43.

Vogtle LK. Pain in adults with cerebral palsy: impact and solutions. Dev Med Child Neurol. 2009;51 Suppl 4:113-21.

Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Joint-position sense and kinesthesia in cerebral palsy. Arch Phys Med Rehabil. 2009;90(3):447-53.

TABLE LEGENDS

Table I. Clinical characteristics of individuals with cerebral palsy. (M=male, F=female, BS=bilateral spastic, D=dyskinetic, A=ataxic).

Table II. Example of activities composing the typical development of somatosensory therapy sessions in one week.

Table III. Mean and standard deviation scores of tactile and pressure pain thresholds before the sensitivity intervention (BI), one week after the sensitivity intervention (AI) and three months after the end of the intervention (PI) at the examined body locations.

Table I.

ID	Group	Sex	Age	CP subgroup	GMFCS	MACS	Mental retardation
1	I	F	32	A	1	1	Mild
2	I	M	33	BS	5	4	Mild
3	I	M	41	A	2	1	Mild
4	I	M	27	D	4	4	None
5	I	F	29	BS	2	1	Mild
6	I	M	31	D	4	3	Mild
7	I	M	36	BS	4	3	Mild
8	I	M	31	BS	2	2	None
9	I	M	26	D	4	3	None
10	I	M	35	BS	5	5	None
11	I	M	25	BS	4	4	None
12	I	M	24	A	1	1	Mild
13	I	F	32	BS	2	5	None
14	I	F	25	A	1	1	Mild
15	I	F	24	BS	4	1	Moderate
16	I	M	34	BS	2	4	None
17	I	M	32	BS	2	4	None

Table II.

	Session 1	*Session 2*
Tactile tasks	Textures in forearms and hands, face and lips Sensitive massage in hands, face and lips	Pressure of different intensity in arms and hand Tactile location exercises in hands, fingers, face and lips Two point discrimination in hands, fingers, face and lips Intraoral work with different textures Intraoral sensitive massage
Propioceptive tasks	Pushing exercises with different weights Following a path with the arms and conciousness of movement Gesticulation and muscular conciouness with mirrow	Body conciousness in upper limb movements without mirrow and with different weights Controlling weigh in a mobile surface Discrimination of velocity of movement in upper limbs
Vibration stimulation	Stimulation of forearms, hands and face	Stimulation of finger, lips and mouth with higher and lower frequencies
Sterognosis	Sterognosis with common objects showed previously	Sterognosis with unseen common objects Sterognosis and description of non-common objects

Table III.

	Tactile threshold			Pain threshold		
	BI	AI	PI	BI	AI	PI
Right lip	*5.29 (2.59)*	*5.35 (2.21)*	*5.00 (2.94)*	***1.07 (1.06)***	***1.76 (1.20)****	***1.56 (1.03)****
Left lip	*6.82 (4.02)*	*5.47 (2.15)*	*4.71 (2.11)*	***3.01 (1.26)***	***1.81 (1.18)*****	***1.63 (1.12)******
Right cheek	*6.76 (3.01)*	*6.00 (3.16)*	*6.35 (4.15)*	***1.39 (0.95)***	***2.48 (1.48)*******	***2.16 (1.31)******
Left cheek	***7.29 (3.85)***	***5.76 (2.61)*****	*7.12 (3.72)*	***1.46 (1.26)***	***2.97 (1.67)*******	***2.16 (1.31)****
Right thenar eminence	***9.88 (4.57)***	***8.47 (4.37)****	*9.47 (4.68)*	***4.17 (2.01)***	***6.85 (3.29)*****	***6.15 (3.04)******
Left thenar eminence	*10,71 (4.75)*	*9.24 (3.87)*	*10.59 (5.78)*	***3.71 (5.34)***	***7.04 (2.91)*******	***5.34 (2.20)******
Right thumb	*8.82 (4.49)*	*8.53 (4.67)*	*10.06 (5.25)*	***4.02 (2.84)***	***5.91 (2.17)*****	***6.07 (3.01)******
Left thumb	***10.12 (4.83)***	***8.00 (3.26)****	*10.71 (5.18)*	***3.95 (2.55)***	***6.57 (3.02)*******	***5.83 (2.82)******
Right index finger	*9.35 (4.66)*	*8.94 (4.63)*	*9.59 (5.66)*	***4.49 (2.98)***	***7.08 (3.49)*******	*5.65 (3.05)*
Left index finger	*9.47 (5.39)*	*8.65 (4.26)*	*10.76 (5.75)*	***3.01 (1.26)***	***6.67 (3.07)*******	***5.51 (2.69)******
Back of the right hand	***10.53 (4.75)***	***8.47 (4.39)****	*9.06 (4.76)*	***3.74 (2.17)***	***6.79 (3.22)*******	***5.45 (3.51)****
Back of the left hand	***11.12 (4.33)***	***9.35 (4.00)****	***9.53 (5.27)****	***3.14 (1.55)***	***6.85 (2.93)*******	***5.27 (2.84)******

* p<.05, **p<.01, ***p<.001

IV

Discusión general de los resultados

El objetivo general de nuestra investigación era examinar los posibles déficits en la percepción y procesamiento somatosensorial que presentan las personas con parálisis cerebral y su relación con los posibles déficits motores de este colectivo. A lo largo de la investigación hemos corroborado la existencia de trastornos somestésicos en personas con parálisis cerebral de todas las edades. Estos trastornos se caracterizaban por la asociación de déficits de propiocepción, una sensibilidad táctil disminuida y una sensibilidad dolorosa aumentada, que no variaban con la edad. Además, el procesamiento de los estímulos somestésicos táctiles presentó asimetrías hemisféricas que se manifestaron distintas según cual fuera el hemicuerpo en el que predominaba la afectación motora. Las personas con parálisis cerebral presentaron además, deficiencias en el periodo de planificación motora. Por último, se examinó si un programa de intervención exclusivamente somatosensorial podría mejorar alguno de los síntomas sensomotores que presentan los pacientes con parálisis cerebral y los resultados preliminares parecen indicar que resulta efectivo para reducir la sensibilidad dolorosa en este colectivo de individuos.

La hipótesis de que la parálisis cerebral se sustenta sobre déficits sensoriomotores representa un avance relevante con respecto a la definición clásica de parálisis cerebral, que apuntaba como principales resultados del daño neurológico a problemas motores como alteraciones del tono muscular, alteraciones de la coordinación y alteraciones de la postura y del movimiento (Krigger, 2006). Esta concepción tradicional de que los problemas prioritarios producidos por la lesión en un SNC en desarrollo eran motores, propició la asunción de que las principales estructuras cerebrales afectadas eran las estructuras relacionadas con la ideación y ejecución motora y con las vías de transmisión del tracto corticoespinal (Son et al., 2007; Staudt et al., 2003). Tras los datos neurofisiológicos apuntando a que las fibras aferentes somatosensoriales se encuentran en muchas ocasiones más dañadas que las fibras eferentes motoras (Yoshida et al., 2010; Hoon et al., 2009, 2002), la perspectiva con la que se contemplaba la patología se ha ampliado, abriendose paso de forma gradual la teoría de que las consecuencias clínicas de la parálisis cerebral son producto de la relación entre los déficits motores y somatosensoriales. El resultado global de nuestra investigación, donde se encontraron múltiples déficits motores y somatosensoriales que se relacionaban entre sí en personas con esta patología, apoya esta teoría.

Nuestros estudios han mostrado que las personas con parálisis cerebral presentan déficits somatosensoriales en mayor medida que la población sana. En primer lugar, tanto la propiocepción como la sensibilidad táctil se encontraron disminuidas. Este resultado coincide con resultados previos de otros autores que publicaron déficits de propiocepción, esterognosia, discriminación entre dos puntos y sensibilidad vibratoria en personas con parálisis cerebral (Wingert et al., 2009, 2008; Sanger&Kukke, 2007; McLaughlin et al., 2005; Cooper et al., 1995; Yekutiel et al., 1994; Lesny et al.1993; Van Heest et al., 1993). Por otra parte, nuestros resultados también mostraron que la percepción dolorosa en las personas con parálisis cerebral es mayor que la de personas sanas de su misma edad. Este resultado también corrobora los datos de la literatura, que hablan de alta incidencia de dolor en las población con parálisis cerebral (Parkes et al., 2009; Russo et al., 2008; Gallien et al., 2007; Odding et al., 2006; Tervo et al., 2006; Engel et al., 2005; Jahnser et al., 2004; Engel et al., 2003; Breau et al., 2003). Algunos autores han afirmado que los procedimientos sanitarios a los que son sometidos las personas con parálisis cerebral de forma habitual, son importantes fuentes de dolor (Lannin et al., 2008; McKearnan et al., 2004; Hadden &Von Baeyer, 2002; Kibele, 1989). Nuestros resultados confirman que algunas técnicas empleadas de forma habitual en los tratamientos de Fisioterapia, producen dolor de moderada intensidad. Este hecho puede ser de una importancia capital, ya que la anormal percepción somatosensorial producida por la patología desde edades tempranas podría, de forma potencial, causar cambios a largo plazo en el procesamiento de la información sensitiva y dolorosa y llevar a una perpetuación del dolor a lo largo del tiempo (Schmelzle-Lubiecki et al., 2007). Asimismo, nuestros resultados mostraron que las personas con parálisis cerebral, al contrario de lo que ocurre con los voluntarios sanos, presentaban una asociación entre una disminución de la sensibilidad táctil y un aumento de la sensibilidad ante estímulos dolorosos. Este resultado sugiere que los mecanismos que regulan la percepción dolorosa en las personas con parálisis cerebral podrían ser distintos a los de otras patologías que cursan con dolor crónico y que experimentan fenómenos como la alodinia (Keizer et al, 2006).

Curiosamente, nuestra investigación probó que la edad era un factor diferencial importante entre la población con parálisis cerebral y la población sana. Así, mientras que los voluntarios sanos mostraron cambios en los parámetros de percepción táctil o dolorosa asociados a su edad, estos cambios no se producían en las personas con

parálisis cerebral. Este resultado contrasta con los de otros autores, que sí observaron cambios en la intensidad del dolor asociados a la edad en personas con parálisis cerebral, aunque de forma contradictoria (Breau et al., 2003; Schwartz et al., 1999). Este descubrimiento sugiere la existencia de mecanismos neurofisiológicos distintos a los de la población sana para el mantenimiento de altos niveles de dolor a lo largo de los años y pone de relevancia la importancia de una valoración y tratamiento específicos y sistemáticos tanto de la sensibilidad somatosensorial como del dolor desde edades tempranas y a lo largo de todo el ciclo vital en las personas con parálisis cerebral. A este respecto, nuestra investigación mostró que un programa de terapia somatosensorial era efectivo para mejorar la sensibilidad dolorosa de adultos con parálisis cerebral. Dada la alta incidencia y de la negativa repercusión que el dolor tiene en la calidad de vida de estas personas (Bjornson et al., 2008; Arnaud et al., 2008; Castle et al., 2007; Dickinson et al., 2007; Jahnser et al., 2004; Engel et al., 2003), este descubrimiento resulta de especial relevancia. Además, estos resultados sugieren la intrigante posibilidad de que los bajos umbrales ante el dolor exhibidos por las personas con parálisis cerebral estén relacionados con la falta de experiencias táctiles. La hiperalgesia producida por reducidos niveles de aferencias constituyó el marco teórico sobre el que Yaksh et al. (1999) realizaron sus trabajos sobre biología medular. También en este sentido, Waldenström et al. (2003) demostraron en experimentos con roedores que las aferencias procedentes de estímulos tactiles podían utilizarse para guiar la organización sináptica del sistema nociceptivo en momentos tempranos del desarrollo. Si admitimos que la plasticidad dependiente de la actividad puede influir en la evolución de los síntomas clínicos (Eyre, 2007), podemos afirmar que la mejora de los umbrales dolorosos y su mantenimiento a lo largo del tiempo obtenidos en nuestro estudio, podrían reflejar cambios en la organización del procesamiento de la información dolorosa. Estos interesantes resultados hacen necesarios nuevos estudios que puedan determinar los efectos neurofisiológicos de la terapia somatosensorial.

Otro interesante resultado que comenzaba a apuntar hacia una relación entre las alteraciones somatosensoriales y motoras en la parálisis cerebral, fue la presencia de una cierta asimetría cerebral en el procesamiento somatosensorial de estímulos táctiles en las personas con parálisis cerebral al estimular hemicuerpos distintos, fenómeno que no aparecía en los sujetos sanos. En concreto, en las personas con parálisis cerebral, las amplitudes de los potenciales evocados somestésicos eran mayores al estimular la parte

del cuerpo más afectada motrizmente. Además aparecieron diferencias en la activación del hemisferio contralateral o ipsilateral al estímulo táctil, relacionadas con el hemicuerpo en el que predomina la afectación motora. Estos datos podrían reflejar una reorganización cortical, en la que el hemicuerpo más afectado motrizmente pudiera haber alterado su representación en la corteza somatosensorial contralateral, tal como se ha demostrado que ocurre en otras patologías como en el ictus (Floel et al., 2008), la distonía focal (Elbert et al., 1998), o la amputación de miembros (Montoya et al., 1998). Así pues, la disfunción motora podría estar modulando la reorganización de la corteza somatosensorial en personas con parálisis cerebral.

El análisis de la acción motora en personas sanas y en personas con parálisis cerebral que presentaron déficits somatosensoriales mostró que las personas con parálisis cerebral presentaban alteraciones en el periodo previo a la contracción muscular, donde presentaron mayores tiempos de reacción, menor amplitud en los potenciales evocados motores y menor coherencia corticomuscular que las personas sanas. Estas alteraciones del periodo de precontracción que encontramos en las personas con parálisis cerebral, parecen indicar problemas en la planificación y programación de la contracción muscular. Otros autores ya han señalado deficiencias en el control anticipatorio de los movimientos en las personas con parálisis cerebral (Steenbergen et al., 2007; Steenbergen & Gordon, 2006; Mutsaarts et al., 2006, 2005). Dada la importancia de la implicación de la corteza somatosensorial en la preparación del acto motor (Pidoux et al., 2010; Haller et al., 2010; Boudreau et al., 2010, Vidoni et al., 2010), es comprensible que la ausencia de un sistema somatosensorial íntegro, tenga repercusiones en la planificación del movimiento (Lourenço et al., 2007; Schmelzle-Lubiecki et al., 2007, Abbruzzese & Berardelli, 2003). Se ha demostrado además la gran influencia que ejerce una correcta información somatosensorial en el aprendizaje de los movimientos (Vidoni & Boyd, 2009; Clarac et al., 2004). Parece pues lógico, que un sistema somatosensorial deficitario desde etapas tempranas de la vida, como es el caso de la parálisis cerebral, tenga influencia en el aprendizaje y preparación del acto motor. Nuestros resultados apuntan en este sentido y refuerzan nuestra hipótesis inicial de que los déficits de la parálisis cerebral podrían sustentarse en un déficit sensoriomotor.

En general, nuestros datos sugieren una íntima relación entre los déficits somatosensoriales y motores en la parálisis cerebral. La confirmación de que la hipótesis del déficit sensoriomotor en la parálisis cerebral es plausible y la

comprobación de que los mecanismos de reorganización plástica se desarrollan en dos sentidos, el que ocurre tras la lesión y el que ocurre tras la terapia, pueden constituir claves importantes en el diseño de futuras estrategias de rehabilitación. En concreto, nuestros resultados destacan la importancia de implementar programas específicos y sistemáticos de valoración y tratamiento, no sólo de los trastornos motores, sino también del dolor y de los déficits somatosensoriales desde edades tempranas y a lo largo de todo el ciclo vital en las personas con parálisis cerebral.

V

Conclusiones

Nuestra investigación ha estudiado las características sociodemográficas de la existencia de déficits somatosensoriales en las personas con parálisis cerebral, las características del procesamiento somatosensorial y motor que presentan personas con esta patología y la eficacia de la terapia somatosensorial en la mejora de estos trastornos. Del análisis de los datos de nuestra investigación podemos extraer las siguientes conclusiones:

1. Las personas con parálisis cerebral presentan dolor y déficits somatosensoriales (táctiles y propioceptivos) que ya están presentes en edades tempranas.

2. La percepción dolorosa aumentada se asocia a una sensibilidad táctil aumentada en las personas sanas, mientras que en las personas con parálisis cerebral, una alta intensidad dolorosa se relaciona con una sensibilidad táctil reducida.

3. Las intervenciones sanitarias a las que habitualmente se someten las personas con parálisis cerebral son consideradas importantes fuentes de dolor, dolor correctamente detectado por los profesionales sanitarios (fisioterapeutas), al que se aproximan con intervenciones poco especificas.

4. La percepción somatosensorial no está influida por la edad en la población con parálisis cerebral, al contrario de lo que ocurre en la población sana.

5. Existen asimetrías cerebrales en el procesamiento somatosensorial de las personas con parálisis cerebral al estimular hemicuerpos distintos. Estas asimetrías no aparecen en las personas sanas.

6. Existen diferencias en la utilización hemisférica para el procesamiento de estímulos tactiles relacionadas con el hemicuerpo en el que predomina la afectación motora.

7. El procesamiento de acciones motoras en personas con parálisis cerebral que presentan déficits somatosensoriales presenta alteraciones, ante todo, en el periodo previo a la contracción muscular.

8. La terapia sensoriomotora puede resultar un instrumento eficaz en la mejora de la sensibilidad dolorosa de personas adultas con parálisis cerebral.

9. Nuestros datos sugieren una estrecha relación entre los déficits somatosensoriales y motores en la parálisis cerebral y destacan la importancia de implementar programas específicos y sistemáticos de valoración y tratamiento, no sólo de los trastornos motores, sino también del dolor y de los déficits

somatosensoriales desde edades tempranas y a lo largo de todo el ciclo vital en las personas con parálisis cerebral.

Aunque esta investigación ha profundizado en la relación entre los trastornos somatosensoriales y motores en las personas con parálisis cerebral, todavía existen numerosas cuestiones sin resolver. De esta forma, el estudio de la posible afectación en otros procesos sensoriales, como la discriminación o la habituación al estímulo, podría proporcionar claves relevantes en el proceso de mantenimiento del dolor a lo largo del tiempo. En esta investigación se han analizado principalmente la sensilibidad táctil y dolorosa, pero la influencia de otros sistemas somatosensoriales se ha considerado sólo de forma secundaria. Sería interesante profundizar en la influencia de la propiocepción en la acción motora, ya que la propiocepción constituye una percepción fundamental para el reconocimiento del propio cuerpo y del movimiento y de forma recurrente se ha demostrado afectada en personas con parálisis cerebral. Asimismo, nuestros estudios hasta el momento se han basado sólo en el análisis de señales procedentes de la corteza cerebral, aunque las lesiones de la parálisis cerebral también afectan a otras estructuras que determinan la forma clínica y que, sin duda, influyen en el procesamiento cortical. Por esta razón, el estudio de la influencia de las lesiones de las estructuras subcorticales en el procesamiento de las aferencias somestésicas y de las eferencias motoras ayudaría a una mayor comprensión de la fisiopatología de la parálisis cerebral.

Siguiendo la doble estructura de esta investigación, que contempla la aplicación clínica de los descubrimientos neurofisiológicos, futuros estudios tendrían también que analizar en qué grado los profesionales que atienden a las personas con parálisis cerebral utilizan la valoración y tratamiento del dolor y la sensibilidad somestésica en la práctica clínica diaria. Si se tiene en cuenta, como se ha sugerido, que muchas intervenciones terapéuticas a las que se someten las personas con parálisis cerebral, son fuentes de dolor, sería necesario determinar la efectividad y eficacia de las distintas intervenciones terapéuticas que previenen y tratan el dolor en esta población. Además, se tendría que ampliar la investigación, con diseños aleatorizados, sobre la eficacia de la terapia sensoriomotora descrita en la presente investigación para mejorar la sensibilidad y la función motora de personas con parálisis cerebral en todas las franjas de edad.

La aceptación de que la parálisis cerebral se sustenta en un déficit sensoriomotor más que en un transtorno exclusivamente motor, abre un nuevo horizonte tanto en los

estudios de plasticidad cerebral como en las estrategias de rehabilitación dirigidas a esta población. Esta tesis pretende ser el inicio de una aproximación a este nuevo concepto, en el que todavía existen numerosas cuestiones sin resolver y en el que, sin duda, surgirán nuevas preguntas. El intentar darles respuesta en un futuro puede ayudar a ampliar el conocimiento general del funcionamiento cerebral tras una lesión y ante todo, puede aportar un pequeño grano de arena para que las personas con parálisis cerebral puedan ver aumentada la calidad de sus tratamientos y disfruten de una mayor funcionalidad y calidad de vida.

VI

Referencias bibliográficas

A

Abbruzzese G, Berardelli A. Sensorimotor integration in movement disorders. Mov Disord. 2003;18(3):231-40.

Arnaud C, White-Koning M, Michelsen SI, Parkes J, Parkinson K, Thyen U, Beckung E, Dickinson HO, Fauconnier J, Marcelli M, McManus V, Colver A. Parent-reported quality of life of children with cerebral palsy in Europe. Pediatrics. 2008;121(1):54-64.

B

Babiloni C, Capotosto P, Del Percio C, Babiloni F, Petrini L, Buttiglione M, Cibelli G, Marusiak J, Romani GL, Arendt-Nielsen L, Rossini PM. Sensorimotor interaction between scomatosensory painful stimuli and motor sequences affects both anticipatory alpha rhythms and behavior as a function of the event side. Brain Res Bull. 2010;81(4-5):398-405.

Barra J, Marquer A, Joassin R, Reymond C, Metge L, Chauvineau V, Pérennou D. Humans use internal models to construct and update a sense of verticality. Brain. 2010;133(Pt 12):3552-63.

Bax M, Goldstein M, Rosenbaum P, Leviton A, Paneth N, Dan B, et al. Executive Committee for the Definition of Cerebral Palsy. Proposed definition and classification of cerebral palsy, April 2005. Dev Med Child Neurol 2005; 47: 571-6.

Berrin SJ, Malcarne VL, Varni JW, Burwinkle TM, Sherman SA, Artavia K, Chambers HG. Pain, fatigue, and school functioning in children with cerebral palsy: a path-analytic model. J Pediatr Psychol. 2007;32(3):330-7.

Bjornson KF, Belza B, Kartin D, Logsdon R, McLaughlin J, Thompson EA. The relationship of physical activity to health status and quality of life in cerebral palsy. Pediatr Phys Ther. 2008;20(3):247-53.

Bleton JP, Vidailhet M, Bourdain F, Ducorps A, Schwartz D, Delmaire C, Lehéricy S, Renault B, Garnero L, Meunier S. Somatosensory cortical remodelling after rehabilitation and clinical benefit of in writer's cramp. J Neurol Neurosurg Psychiatry. 2011;82(5):574-7.

Boćkowski L, Okurowska-Zawada B, Sobaniec W, Kułak W, Sendrowski K. Cortical somatosensory evoked potentials and spasticity assessment after botulinum toxin type A injection in children with cerebral palsy. Adv Med Sci. 2007;52 Suppl 1:171-5.

Borsook D, Upadhyay J, Chudler EH, Becerra L. A key role of the basal ganglia in pain and analgesia--insights gained through human functional imaging. Mol Pain. 2010;6:27.

Boudreau S, Romaniello A, Wang K, Svensson P, Sessle BJ, Arendt-Nielsen L. The effects of intra-oral pain on motor cortex neuroplasticity associated with short-term novel tongue-protrusion training in humans. Pain. 2007;132(1-2):169-78.

Boudreau SA, Hennings K, Svensson P, Sessle BJ, Arendt-Nielsen L. The effects of training time, sensory loss and pain on human motor learning. J Oral Rehabil. 2010;37(9):704-18.

Breau LM, Camfield CS, McGrath PJ, Finley GA. The incidente of pain in children with severe cognitive impairments. Arch Pediatr Adolesc Med. 2003;157(12):1219-26.

Briellmann RS, Abbott DF, Caflisch U, Archer JS, Jackson GD. Brain reorganisation in cerebral palsy: a high-field functional MRI study. Neuropediatrics. 2002;33(3):162-5.

C

Cans C. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Dev Med Child Neurol. 2000;42(12):816-24.

Castle K, Imms C, Howie L. Being in pain: a phenomenological study of young people with cerebral palsy. Dev Med Child Neurol. 2007;49(6):445-9.

Cherng RJ, Su FC, Chen JJ, Kuan TS. Performance of static standing balance in children with spastic diplegic cerebral palsy under altered sensory environments. Am J Phys Med Rehabil. 1999;78(4):336-43.

Clarac F, Brocard F, Vinay L. The maturation of locomotor networks. Prog Brain Res. 2004; 143: 57–66.

Clayton K, Fleming JM, Copley J. Behavioral responses to tactile stimuli in children with cerebral palsy. Phys Occup Ther Pediatr. 2003;23(1):43-62.

Cooper J, Majnemer A, Rosenblatt B, Birnbaum R. The determination of sensory deficits in children with hemiplegic cerebral palsy. J Child Neurol. 1995;10(4):300-9.

Coq JO, Strata F, Russier M, Safadi FF, Merzenich MM, Byl NN, Barbe MF. Impact of neonatal asphyxia and hind limb immobilization on musculoskeletal tissues and S1 map organization: Implications for cerebral palsy. Experimental Neurology 2008; 210: 95–108.

Curry J, Exner C. Comparison of tactile preferences in children with and without cerebral palsy. Am J Occup Ther. 1988;42(6):371-7.

D

Doralp S, Bartlett DJ. The prevalence, distribution, and effect of pain among adolescents with cerebral palsy. Pediatr Phys Ther. 2010;22(1):26-33.

Dudgeon BJ, Gerrard BC, Jensen MP, Rhodes LA, Tyler EJ. Physical disability and the experience of chronic pain. Arch Phys Med Rehabil. 2002;83(2):229-35.

Duff SV, Gordon AM. Learning of grasp control in children with hemiplegic cerebral palsy. Dev Med Child Neurol. 2003;45(11):746-57.

E

Ekert PG, Taylor MJ, Keenan NK, Boulton JE, Whyte HE. Early somatosensory evoked potentials in preterm infants: their prognostic utility. Biol Neonate. 1997;71(2):83-91.

Elbert T, Candia V, Altenmüller E, Rau H, Sterr A, Rockstroh B, Pantev C, Taub E. Alteration of digital representations in somatosensory cortex in focal hand dystonia. Neuroreport. 1998;9(16):3571-5.

Eliasson AC, Gordon AM, Forssberg H. Basic co-ordination of manipulative forces of children with cerebral palsy. Dev Med Child Neurol. 1991;33(8):661-70.

Engel JM, Jensen MP, Hoffman AJ, Kartin D. Pain in persons with cerebral palsy: extension and cross validation. Arch Phys Med Rehábil. 2003;84:1125–1128.

Engel JM, Petrina TJ, Dudgeon BJ, McKearnan KA. Cerebral palsy and chronic pain: a descriptive study of children and adolescents. Phys Occup Ther Pediatr. 2005;25(4):73-84.

Eyre JA. Corticospinal tract development and its plasticity after perinatal injury. Neurosci Biobehav Rev. 2007;31(8):1136-49.

F

Floel A, Hummel F, Duque J, Knecht S, Cohen LG. Influence of somatosensory input on interhemispheric interactions in patients with chronic stroke. Neurorehabil Neural Repair. 2008;22(5):477-85.

Flor H. Remapping somatosensory cortex after injury. Adv Neurol. 2003;93:195-204.

Frascarelli F, Di Rosa G, Bisozzi E, Castelli E, Santilli V. Neurophysiological changes induced by the botulinum toxin type A injection in children with cerebral palsy. Eur J Paediatr Neurol. 2011;15(1):59-64.

G

Gainsborough M, Surman G, Maestri G, Colver A, Cans C. Validity and reliability of the guidelines of surveillance of cerebral palsy in Europe for the classification of cerebral palsy. Dev Med Child Neurol. 2008; 50(11):828:31.

Galea MP, Darian-Smith I. Multiple corticospinal neuron populations in the macaque monkey are specified by their unique cortical origins, spinal terminations, and connections. Cereb Cortex. 1994;4(2):166-94.

Gallien P, Nicolas B, Dauvergne F, Pétrilli S, Houedakor J, Roy D, Duruflé A. Pain in adults with cerebral palsy Ann Readapt Med Phys. 2007;50(7):558-63.

Gerloff C, Braun C, Staudt M, Hegner YL, Dichgans J, Krägeloh-Mann I. Coherent corticomuscular oscillations originate from primary motor cortex: evidence from patients with early brain lesions. Hum Brain Mapp. 2006;27(10):789-98.

Gibson NA, Graham M, Levene MI. Somatosensory evoked potentials and outcome in perinatal asphyxia. Arch Dis Child. 1992;67(4 Spec No):393-8.

Gordon AM, Charles J, Steenbergen B. Fingertip force planning during grasp is disrupted by impaired sensorimotor integration in children with hemiplegic cerebral palsy. Pediatr Res. 2006;60(5):587-91.

Görke W. Somatosensory evoked cortical potentials indicating impaired motor development in infancy. Dev Med Child Neurol. 1986;28(5):633-41.

H

Hadden KL, von Baeyer CL. Pain in children with cerebral palsy: common triggers and expressive behaviors. Pain. 2002;99(1-2):281-8.

Haller S, Chapuis D, Gassert R, Burdet E, Klarhöfer M. Supplementary motor area and anterior intraparietal area integrate fine-graded timing and force control during precision grip. Eur J Neurosci. 2009;30(12):2401-6.

Hilberink SR, Roebroeck ME, Nieuwstraten W, Jalink L, Verheijden JM, Stam HJ. Health issues in young adults with cerebral palsy: towards a life-span perspective. J Rehabil Med. 2007;39(8):605-11.

Hoon AH Jr, Lawrie WT Jr, Melhem ER, Reinhardt EM, Van Zijl PC, Solaiyappan M, Jiang H, Johnston MV, Mori S. Diffusion tensor imaging of periventricular leukomalacia shows affected sensory cortex white matter pathways. Neurology. 2002;59(5):752-6.

Hoon AH Jr, Stashinko EE, Nagae LM, Lin DD, Keller J, Bastian A, Campbell ML, Levey E, Mori S, Johnston MV. Sensory and motor deficits in children with cerebral palsy born preterm correlate with diffusion tensor imaging abnormalities in thalamocortical pathways. Dev Med Child Neurol. 2009;51(9):697-704.

Houlihan CM, O'Donnell M, Conaway M, Stevenson RD. Bodily pain and health-related quality of life in children with cerebral palsy. Dev Med Child Neurol. 2004;46(5):305-10.

I

Iseki K, Hanakawa T, Hashikawa K, Tomimoto H, Nankaku M, Yamauchi H, Hallett M, Fukuyama H. Gait disturbance associated with white matter changes: a gait analysis and blood flow study. Neuroimage. 2010 Jan 15;49(2):1659-66.

Ito M, Okuno T, Takao T, Konishi Y, Yoshioka M, Mikawa H. Electroencephalographic and cranial computed tomographic findings in children with hemiplegic cerebral palsy. Eur Neurol. 1981;20(4):312-8.

J

Jahnsen R, Villien L, Aamodt G, Stanghelle JK, Holm I. Musculoskeletal pain in adults with cerebral palsy compared with the general population. J Rehabil Med. 2004;36(2):78-84.

Jóźwiak M, Harasymczuk P, Koch A, Kotwicki T. Incidence and risk factors of hip joint pain in children with severe cerebral palsy. Disabil Rehabil. 2011;33(15-16):1367-72.

K

Keizer D,Fael D, Wierda JM, van Wijhe M. Quantitative sensory testing with Von Frey monofilaments in patients with allodynia: what are we quantifying? Clin J Pain 2008;24:463-466.

Kennes J, Rosenbaum P, Hanna SE, Walter S, Russell D, Raina P, Bartlett D, Galuppi B. Health status of school-aged children with cerebral palsy: information from a population-based sample. Dev Med Child Neurol. 2002;44(4):240-7.

Kerem M, Livanelioglu A, Topcu M. Effects of Johnstone pressure splints combined with neurodevelopmental therapy on spasticity and cutaneous sensory inputs in spastic cerebral palsy. Dev Med Child Neurol. 2001;43(5):307-13.

Kibele A. Occupational therapy's role in improving the quality of life for persons with cerebral palsy. Am J Occup Ther. 1989;43(6):371-7.

Kirimoto H, Ogata K, Onishi H, Oyama M, Goto Y, Tobimatsu S. Clin Neurophysiol. Transcranial direct current stimulation over the motor association cortex induces plastic changes in ipsilateral primary motor and somatosensory cortices. 2011;122(4):777-83.

Krägeloh-Mann I, Cans C. Cerebral palsy update. Brain Dev. 2009;31(7):537-44.

Krigger KW. Cerebral palsy: an overview. Am Fam Physician. 2006;73(1):91-100.

Kułak W, Sobaniec W, Boćkowski L. EEG spectral analysis and coherence in children with hemiparetic cerebral palsy. Med Sci Monit. 2005;11(9):CR449-55.

L

Lannin NA, Novak I, Cusick A. A systematic review of upper extremity casting for children and adults with central nervous system motor disorders. Clin Rehabil. 2007;21(11):963-76.

LaPointe KE, Klein JA, Konkol ML, Kveno SM, Bhatt E, DiFabio RP, Carey JR. Cortical activation during finger tracking vs. ankle tracking in healthy subjects. Restor Neurol Neurosci. 2009;27(4):253-264.

Lesný I, Stehlík A, Tomásek J, Tománková A, Havlícek I. Sensory disorders in cerebral palsy: two-point discrimination. Dev Med Child Neurol. 1993;35(5):402-5.

Lourenço G, Meunier S, Vidailhet M, Simonetta-Moreau M. Impaired modulation of motor cortex excitability by homonymous and heteronymous muscle afferents in focal hand dystonia. Mov Disord. 2007;22(4):523-7.

M

Maegaki Y, Maeoka Y, Ishii S, Eda I, Ohtagaki A, Kitahara T, Suzuki N, Yoshino K, Ieshima A, Koeda T, Takeshita K. Central motor reorganization in cerebral palsy patients with bilateral cerebral lesions. Pediatr Res. 1999;45(4 Pt 1):559-67.

Malone LA, Vogtle LK. Pain and fatigue consistency in adults with cerebral palsy. Disabil Rehabil. 2010;32(5):385-91.

McKearnan KA, Kieckhefer GM, Engel JM, Jensen MP, Labvak S. Pain in children with cerebral palsy: a review. J Neurosci Nurs. 2004;36(5):252-9.

McLaughlin JF, Felix SD, Nowbar S, Ferrel A, Bjornson K, Hays RM. Lower extremity sensory function in children with cerebral palsy. Pediatr Rehabil. 2005;8(1):45-52.

Meesen RL, Cuypers K, Rothwell JC, Swinnen SP, Levin O. The effect of long-term TENS on persistent neuroplastic changes in the human cerebral cortex. Hum Brain Mapp. 2011;32(6):872-82.

Montoya P, Ritter K, Huse E, Larbig W, Braun C, Töpfner S, Lutzenberger W, Grodd W, Flor H, Birbaumer N. The cortical somatotopic map and phantom phenomena in subjects with congenital limb atrophy and traumatic amputees with phantom limb pain. Eur J Neurosci. 1998;10(3):1095-102.

Montoya P, Sitges C, Garcia-Herrera M, Rodriguez-Cotes A, Izquierdo R, Truyols M, et al. Reduced brain habituation to somatosensory stimulation in patients with fibromyalgia. Arthritis Rheum 2006;54:1995–2003.

Montoya P, Sitges C. Affective modulation of somatosensory evoked potentials elicited by tactile stimulation. Brain Res 2006;1068(1):205–12.

Moulton EA, Schmahmann JD, Becerra L, Borsook D. The cerebellum and pain: passive integrator or active participator? Brain Res Rev. 2010;65(1):14-27.

Murphy KP. The adult with cerebral palsy. Orthop Clin North Am. 2010;41(4):595-605.

Mutsaarts M, Steenbergen B, Bekkering H. Anticipatory planning deficits and task context effects in hemiparetic cerebral palsy. Exp Brain Res. 2006;172(2):151-62.

Mutsaarts M, Steenbergen B, Bekkering H. Anticipatory planning of movement sequences in hemiparetic cerebral palsy. Motor Control. 2005;9(4):439-58.

N

Nashner LM, Shumway-Cook A, Marin O. Stance posture control in select groups of children with cerebral palsy: deficits in sensory organization and muscular coordination. Exp Brain Res. 1983;49(3):393-409.

O

Odding E, Roebroeck ME, Stam HJ. The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil Rehabil. 2006;28(4):183-91.

Opheim A, Jahnsen R, Olsson E, Stanghelle JK. Walking function, pain, and fatigue in adults with cerebral palsy: a 7-year follow-up study. Ann Readapt Med Phys. 2007;50(1):20-7.

O'Shea M. Cerebral palsy. Semin Perinatol. 2008;32(1):35-41.

Ostry DJ, Darainy M, Mattar AA, Wong J, Gribble PL. Somatosensory plasticity and motor learning. J Neurosci. 2010;30(15):5384-93.

P

Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 1997;39(4):214-23.

Park ES, Park CI, Kim DY, Kim YR. The effect of spasticity on cortical somatosensory-evoked potentials: changes of cortical somatosensory-evoked potentials after botulinum toxin type A injection. Arch Phys Med Rehabil. 2002; 83(11):1592-6.

Parkes J, McCullough N, Madden A, McCahey E. The health of children with cerebral palsy and stress in their parents.J Adv Nurs. 2009;65(11):2311-23.

Parkinson KN, Gibson L, Dickinson HO, Colver AF. Pain in children with cerebral palsy: a cross-sectional multicentre European study. Acta Paediatr. 2010;99(3):446-51.

Peltz E, Seifert F, Decol R, Dörfler A, Schwab S, Maihöfner C. Functional connectivity of the human insular cortex during noxious and innocuous thermal stimulation. Neuroimage. 2011;54(2):1324-35.

Pidoux M, Mahon S, Deniau JM, Charpier S. Integration and propagation of somatosensory responses in the corticostriatal pathway: an intracellular study in vivo. J Physiol. 2011;589(Pt 2):263-81

Pierrat V, Eken P, de Vries LS. The predictive value of cranial ultrasound and of somatosensory evoked potentials after nerve stimulation for adverse

neurological outcome in preterm infants. Dev Med Child Neurol. 1997; 39(6):398-403.

R

Rathelot JA, Strick PL. Muscle representation in the macaque motor cortex: an anatomical perspective. Proc Natl Acad Sci U S A. 2006;103(21):8257-62.

Rosenbaum P, Paneth N, Leviton A, Goldstein M, Bax M, Damiano D, Dan B, Jacobsson B. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl. 2007;109:8-14.

Russo RN, Miller MD, Haan E, Cameron ID, Crotty M. Pain characteristics and their association with quality of life and self-concept in children with hemiplegic cerebral palsy identified from a population register. Clin J Pain. 2008;24(4):335-42.

S

Samani A, Holtermann A, Søgaard K, Madeleine P. Experimental pain leads to reorganisation of trapezius electromyography during computer work with active and passive pauses. Eur J Appl Physiol. 2009;106(6):857-66.

Sanger TD, Kukke SN. Abnormalities of tactile sensory function in children with dystonic and diplegic cerebral palsy. J Child Neurol. 2007;22(3):289-93.

Schmelzle-Lubiecki BM, Campbell KA, Howard RH, Franck L, Fitzgerald M. Long-term consequences of early infant injury and trauma upon somatosensory processing. Eur J Pain. 2007;11(7):799-809.

Schwartz L, Engel JM, Jensen MP. Pain in persons with cerebral palsy. Arch Phys Med Rehabil. 1999;80:1243-1246.

Seki K, Perlmutter SI, Fetz EE. Sensory input to primate spinal cord is presynaptically inhibited during voluntary movement. Nat Neurosci. 2003;6(12):1309-16.

Son SM, Ahn YH, Sakong J, Moon HK, Ahn SH, Lee H, Yu IK, Shin YJ, Jang SH. Diffusion tensor imaging demonstrates focal lesions of the corticospinal tract in hemiparetic patients with cerebral palsy. Neurosci Lett. 2007;420(1):34-8.

Staudt M, Pavlova M, Böhm S, Grodd W, Krägeloh-Mann I. Pyramidal tract damage correlates with motor dysfunction in bilateral periventricular leukomalacia (PVL). Neuropediatrics. 2003;34(4):182-8.

Steenbergen B, Gordon AM. Activity limitation in hemiplegic cerebral palsy: evidence for disorders in motor planning. Dev Med Child Neurol. 2006;48(9):780-3.

Steenbergen B, Hulstijn W, Lemmens IH, Meulenbroek RG. The timing of prehensile movements in subjects with cerebral palsy. Dev Med Child Neurol. 1998;40(2):108-14.

Steenbergen B, Verrel J, Gordon AM. Motor planning in congenital hemiplegia. Disabil Rehabil. 2007;29(1):13-23.

Strata F, Coq JO, Byl N, Merzenich MM. Effects of sensorimotor restriction and anoxia on gait and motor cortex organization: implications for a rodent model of cerebral palsy. Neuroscience. 2004;129(1):141-56.

Suppiej A, Cappellari A, Franzoi M, Traverso A, Ermani M, Zanardo V. Bilateral loss of cortical somatosensory evoked potential at birth predicts cerebral palsy in term and near-term newborns. Early Hum Dev. 2010;86(2):93-8.

T

Tarsuslu T, Livanelioglu A. Relationship between quality of life and functional status of young adults and adults with cerebral palsy. Disabil Rehabil. 2010;32(20):1658-65.

Tervo RC, Symons F, Stout J, Novacheck T. Parental report of pain and associated limitations in ambulatory children with cerebral palsy. Arch Phys Med Rehabil. 2006;87(7):928-934.

Thomas B, Eyssen M, Peeters R, Molenaers G, Van Hecke P, De Cock P, Sunaert S. Quantitative diffusion tensor imaging in cerebral palsy due to periventricular white matter injury. Brain. 2005;128(Pt 11):2562-77.

Turk MA, Geremski CA, Rosembaum PF, Weber RJ. The health status of women with cerebral palsy. Arch Phys Med Rehabil. 1997;78(12 Suppl 5):S10-7.

Turk MA. Health, mortality, and wellness issues in adults with cerebral palsy. Dev Med Child Neurol. 2009;51 Suppl 4:24-9.

Tyč F, Boyadjian A. Plasticity of motor cortex induced by coordination and training. Clin Neurophysiol. 2011;122(1):153-62.

V

Van Elk M, Crajé C, Beeren ME, Steenbergen B, van Schie HT, Bekkering H. Neural evidence for impaired action selection in right hemiparetic cerebral palsy. Brain Res. 2010;1349:56-67.

Van Heest AE, House J, Putnam M. Sensibility deficiencies in the hands of children with spastic hemiplegia. J Hand Surg Am. 1993;18(2):278-81.

Vidoni ED, Acerra NE, Dao E, Meehan SK, Boyd LA. Role of the primary somatosensory cortex in motor learning: An rTMS study. Neurobiol Learn Mem. 2010;93(4):532-9.

Vidoni ED, Boyd LA. Preserved motor learning after stroke is related to the degree of proprioceptive deficit. Behav Brain Funct. 2009;5:36.

Vogtle LK. Pain in adults with cerebral palsy: impact and solutions. Dev Med Child Neurol. 2009;51 Suppl 4:113-21.

W

Waldenström A, Thelin J, Thimansson E, Levinsson A, Schouenborg J. Developmental learning in a pain-related system: evidence for a cross-modality mechanism.J Neurosci. 2003;23(20):7719-25.

Wheaton LA, Nolte G, Bohlhalter S, Fridman E, Hallett M. Synchronization of parietal and premotor areas during preparation and execution of praxis hand movements. Clin Neurophysiol. 2005;116(6):1382-90.

Wilke M, Staudt M. Does damage to somatosensory circuits underlie motor impairment in cerebral palsy? Dev Med Child Neurol. 2009;51(9):686-7.

Wingert JR, Burton H, Sinclair RJ, Brunstrom JE, Damiano DL. Joint-position sense and kinesthesia in cerebral palsy. Arch Phys Med Rehabil. 2009;90(3):447-53.

Witham CL, Wang M, Baker SN. Corticomuscular coherence between motor cortex, somatosensory areas and forearm muscles in the monkey. Front Syst Neurosci. 2010 Jul 30;4. pii: 38.

Wittenberg GF. Motor mapping in cerebral palsy. Dev Med Child Neurol. 2009;51 Suppl 4:134-9.

X

Xie YF, Huo FQ, Tang JS. Cerebral cortex modulation of pain. Acta Pharmacol Sin. 2009;30(1):31-41.

Y

Yaksh TL, Hua XY, Kalcheva I, Nozaki-Taguchi N, Marsala M. The spinal biology in humans and animals of pain states generated by persistent small afferent input. Proc Natl Acad Sci U S A. 1999;96(14):7680-6.

Yekutiel M, Jariwala M, Stretch P. Sensory deficit in the hands of children with cerebral palsy: a new look at assessment and prevalence. Dev Med Child Neurol. 1994;36(7):619-24.

Yoshida S, Hayakawa K, Yamamoto A, Okano S, Kanda T, Yamori Y, Yoshida N, Hirota H. Quantitative diffusion tensor tractography of the motor and sensory tract in children with cerebral palsy. Dev Med Child Neurol. 2010;52(10):935-40

Z

Ziluk A, Premji A, Nelson AJ. Functional connectivity from area 5 to primary motor cortex via paired-pulse transcranial magnetic stimulation. Neurosci Lett. 2010;484(1):81-5.