Universidad de Barcelona

Facultad de Medicina

Departamento de Neurociencias clínicas y experimentales

INTERACCIÓN ENTRE REACCIÓN DE SOBRESALTO Y REACCIÓN VOLUNTARIA EN EL SER HUMANO

Tesis presentada por

HATICE KUMRU

para optar al grado de Doctora en medicina y cirugia

Barcelona, 2009

Directores de la tesis

Dr. Josep Valls-Solé

Dr. Joan Santamaria

Sevgili Marc ve Ramon icin

Bu sure icinde bana tahammul ettiginiz icin tessekkur ediyorum

Agredecimientos

Dr. Josep Valls, thanks for your knowledge, energy, capacity for teaching, for being always available to help, and for being my friend.

Dr Joan Santamaria, thank you for being very gentile, great scientist and wonderful friend.

Dr Tolosa, Dra Marti, Dr Valldeoriola and Dr Muñoz, thanks for accepting me in your department and teaching me on movement disorders.

Dr Markus Kofler, thank you for sharing your scientific knowledge with me and for being my friend.

Doctors who shared their time and experience with me in Hospital Clinic (A Iranzo, M Begeman, P Schestatsky, J Costa, J Casanova, X Urra, Y Compta, S Amaro, JM Castellote, MT Sanegre, L Leon, M Veciana, F Turbau, C Castillo, D Perez)

Institut Guttmann:

Dr Ramirez, thank you for accepting me to work in this hospital where I have been given the possibility to develop my research interests.

Dr Vidal, thank you for your great collaboration and intention to develop research.

Dr Tormos, Dra Amargos, Dra Bernabeu thank you for your help and collaboration.

Dolors; Narda, thanks for your collaboration in many scientific areas and for sharing your research themes and time with me…. and good luck with your thesis.

Doctors, who shared their time and experience with me in Institut Guttmann (Portell, Borau, Benito, Valles, Terre, Guevarra, D Leon, Curia, Pelayo, N Leon, Capdevilla, Castaño, Lage, P Medina).

I want to thank also to the people, who are always helping us in the clinical practice and in research (A Garcia, Eloy, Raquel, Marta).

Olga thank you for your energy to supply me the literature and to help when I needed.

Marilina, Gisela thank you for being patient with me and for your help in the clinical practice.

And thank you, Inmaculada Aso, Luis Subirana, and the rest of my in-laws to be patient during the time needed for preparation of this thesis.

ABBREVIACIONES

RS : la reacción del sobresalto

RSA : la reacción del sobresalto auditivo

IS : el señal imperativo

ESA : el estímulo de sobresalto auditivo

SRT : tiempo de reacción simple

IPP : inhibición por prepulso

RO : la reacción de orientación

nRCP : el núcleo reticular caudal de la protuberancia

PPN : el núcleo peduculopontine

EMT : estimulación magnetica transcraneal

PEM : potencial evocado motor

OOc : el músculo orbicularis oculi

SCM : el músculo esternocleidomastoidea

SC : el colliculus superior

tREF : Tiempo de reacción de elección forzada

Índice

Capítulo 1. - Introducción

1.1. Definición: La reacción de sobresalto y la reacción voluntaria

1.2 . Anatomía funcional de la reacción de sobresalto

1.3. Factores que influencian la magnitud de la reacción de sobresalto

1.4. Reacción de sobresalto e inhibición por prepulso

1.5. Midiendo la excitabilidad del circuito del sobresalto antes de la reacción voluntaria

1.6. La reacción de sobresalto en el contexto de los movimientos

1.1. Definición: La reacción de sobresalto y la reacción voluntaria

Cuando escuchamos un sonido intenso e inesperado podemos tener una reacción de sobresalto (RS) que es común a la mayoría de mamíferos. La respuesta, que se puede dividir en varios componentes, consiste típicamente en extensión seguida de flexión rápidas de una serie de músculos. La figura 1 demuestra el cambio en el cuerpo entero que una rata está experimentando como consecuencia de la presentación de un sonido de alta intensidad. La RS no está generalmente bajo control voluntario, y se puede modificar por muchas intervenciones. Por ejemplo, tanto los humanos como las ratas tienen RS más grande cuando están asustados (Grillon et al. 1991). Este aumento se puede reducir por las medicaciones que reducen la ansiedad (Graham et al. 2005). Si se presentan estímulos en el umbral de percepción (baja intensidad) poco antes de emitir un estímulo acústico, éste produce una reducción en la reacción de sobresalto. Este efecto, conocido como inhibición por prepulso (PPI) es anormal en algunos pacientes psiquiátricos (Takahashi et al. 2008) y nos indica la existencia de circuitos subcorticales usados en el control de la RS. Por estos y otros motivos, los cambios en el tamaño de la RS son ampliamente utilizados para estudiar las sensaciones como el miedo o la ansiedad, y los efectos de información sensorial relevante.

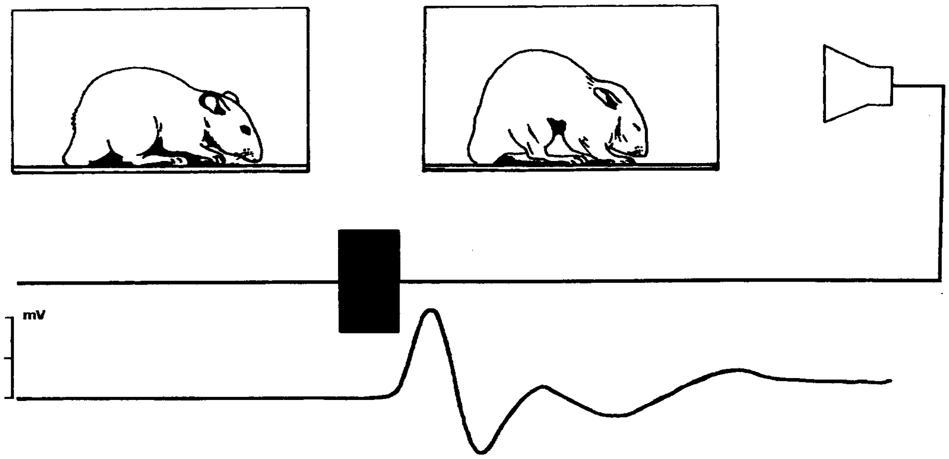
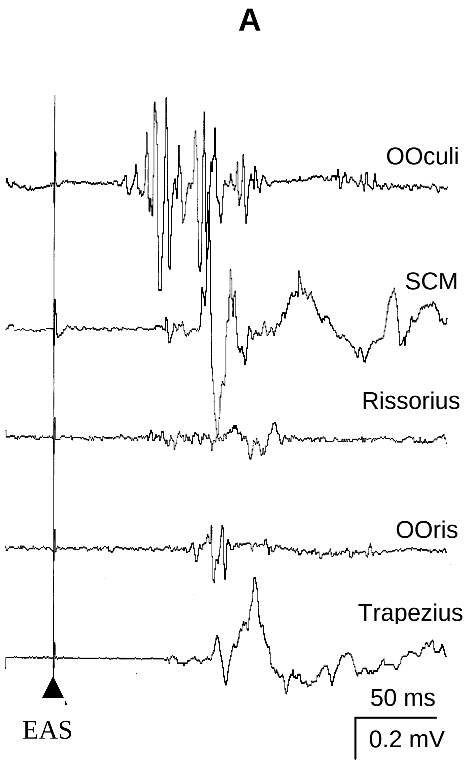


Figura 1. *La respuesta de sobresalto acústico en una rata 30 ms después del inicio del estímulo. Los cuadros están dibujados de acuerdo a una grabación tomada por Carsten Spiekermann (Diploma-tesis inédita en la universidad de Tubingen) con una cámara fotográfica de alta velocidad (150 marcos por segundos). La parte inferior de la figura muestra el balistograma de la RS del cuerpo. La RS se expresa generalmente como unidades arbitrarias o en mVs a partir del registro acelerométrico.*

La RS es la consecuencia de la activación involuntaria de los tractos motores generados en el tronco del encéfalo, principalmente en la formación reticular bulbopontina (Landis y la caza 1939; Davis y Gendelman 1977; Davis et al. 1982; Wilkins et al. 1986; Brown et al. 1991a). La contracción rápida, breve y generalizada de los músculos, típica de la RS, se muestra en la figura 2A para una persona sana. Esta reacción rápida es seguida por una reacción elaborada, llamada reacción de orientación (RO), que se muestra como la contracción de músculos faciales en la figura 2B. La RS tiene una función protectora básica frente a estímulos sensoriales inesperados, mientras que la RO podría estar relacionada con la preparación de la reacción de defensa o ataque, subsecuente al estímulo.



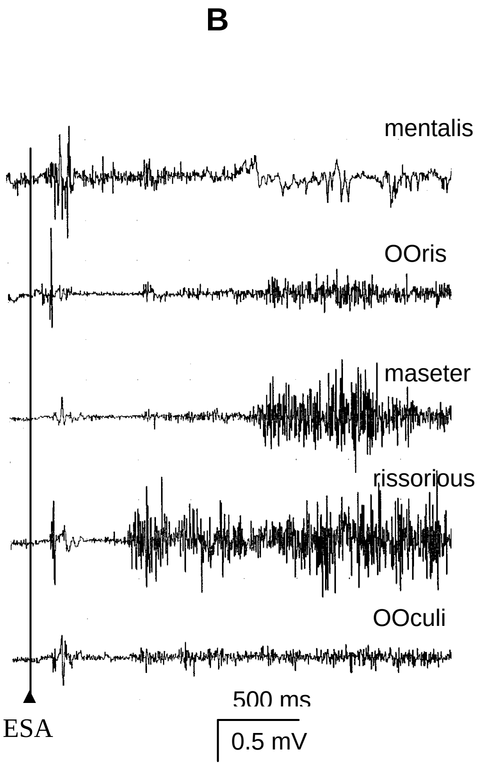


Figura 2A. *La reacción de sobresalto a un estímulo auditivo. La actividad fue registrada en músculos faciales y cervicales con un barrido rápido para mostrar el componente de latencia corta de la RS. EAS: estimulo auditivo capaz de causar una RS.*

Figura 2B. *Reacción de orientación en los músculos faciales*

La RS es la reacción generalizada más rápida del sistema motor en seres humanos y animales. Por ello, sería conveniente utilizar los circuitos del RS para la ejecución de los movimientos que requieren gran velocidad. No obstante, debe existir también un mecanismo de control para evitar efectuar la actividad motora cuando es inconveniente. Probablemente, el mecanismo fisiológico más conocido de control de la RS es la inhibición por prepulso (PPI), que se define como el efecto de inhibición de la respuesta motora que de otra manera causaría un estímulo intenso, cuando se aplica una señal sensorial débil, incapaz por si misma de producir respuesta motora (Graham 1975; Koch et al. 1993; Swerdlow y Geyer 1993; Inglis y Winn 1995).

La ejecución de un acto motor voluntario requiere la activación de circuitos neuronales cerebrales. Los comandos voluntarios se pueden generar en los circuitos que enlazan los ganglios basales y las áreas premotora y motora suplementaria. Sin embargo, si la ejecución rápida del movimiento es necesaria, los seres humanos preparamos generalmente los circuitos motores subcorticales de una manera tal que estén listos para el lanzamiento del programa motor en el momento apropiado, como el corredor a punto para salir en una carrera de 100 m (figura 3). Los mecanismos fisiológicos de la preparación motora subyacente no se conocen pero implican ciertamente una acumulación de la excitabilidad en estructuras subcorticales de acuerdo con el programa que se ejecutará. En tal situación, una entrada sensorial inesperada, suficientemente intensa, puede accionar la respuesta motora por activación directa de las estructuras subcorticales totalmente preparadas, un fenómeno llamado `StartReact' (Valls-Solé et al. 1995; 1999a; Valldeoriola et al., 1998; Carlsen et al. 2004a, b).

Figura 3. *El efecto del estímulo auditivo de sobresalto en la reacción voluntaria contribuye probablemente a acelerar la salida en una carrera de 100 m.*

1.2. Anatomía funcional de la reacción sobresalto

Los estudios en animales han contribuido a aportar información esencial sobre los circuitos implicados en la RS (Davis et al. 1982; Lingenhöhl y Friauf 1994; Yeomans y Frankland 1996; Koch 1999). La respuesta está presente en animales decerebrados a nivel intercollicular (Davis y Gendelman 1977). Generalmente, en seres humanos, la RS está inducida por estímulos auditivos, aunque también se han usado estímulos visuales (McManis et al. 2001), somatosensoriales (Gokin y Karpukhina 1985) o vestibulares (Bisdorff et al. 1994). En la rata, Davis y colaboradores [9] demostraron que la RS puede generarse por estimulación eléctrica directa del núcleo reticular caudal de la protuberancia (nRCP), pero no del núcleo reticular giganto-celular. Por ello, propusieron un circuito para la RS generada por estímulos auditivos consistente en el núcleo coclear, el núcleo del lemnisco lateral, el nRCP y las motoneuronas del tronco cerebral y de la médula espinal por mediación del tracto retículo-espinal medial. Posteriormente, Lingenhohl y Friauf (1994) describieron que el nRCP recibe aferencias del núcleo coclear y Lee et al (1996) mostró que el núcleo del lemnisco lateral no era necesario para la reacción. Actualmente, se considera que la RS se vehicula por un circuito muy simple, compuesto por el núcleo coclear, el nRCP y las motoneuronas alfa (Yeomans y Frankland 1996; Davis 1996; Koch 1999). Las neuronas gigantes del nRCP no son específicas para una determinada modalidad sensorial (Wu et al. 1988) y, por lo tanto, es probable que el mismo circuito esté implicado en la RS inducida por aferencias sensoriales de modalidades distintas de las auditivas.

Algunos autores opinan, sin embargo, que la parte más inicial de la respuesta del músculo orbicular de los párpados es un reflejo auditivo-palpebral, diferente de la RS (Brown et al 1991). Estos autores sugieren que los mecanismos fisiológicos del reflejo auditivo-palpebral son diferentes de los de la RS, y que los circuitos neuronales involucrados son distintos. Este concepto está basado principalmente en el hecho de que la respuesta del músculo orbicular de los párpados es mucho más consistente y fácil de inducir que la RS. A diferencia de la RS, el reflejo auditivo-palpebral podría vehicularse a través del núcleo del colículo inferior y la formación reticular mesencefálica (Hori et al. 1986). La Figura 4 muestra estos dos circuitos.

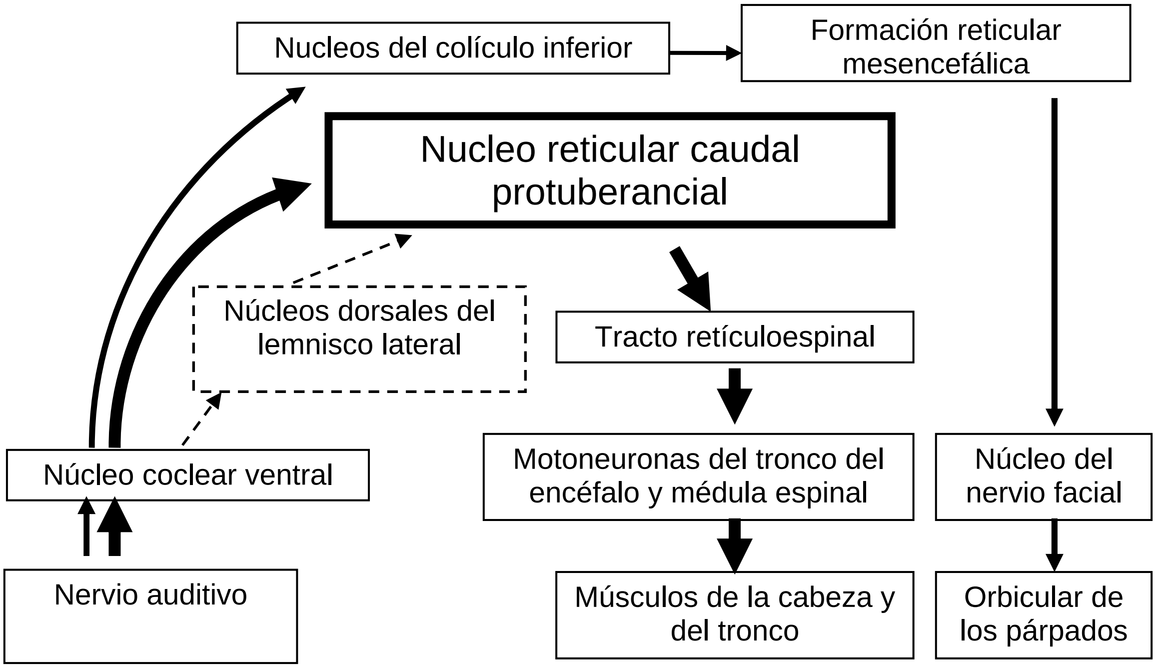


Figura 4. *El circuito de la reacción de sobresalto a estímulos auditivos. Las estructuras que median la reacción de sobresalto según describieron Davis et al. (1982).*

La manifestación más evidente de la RS en seres humanos es su componente temprano: una contracción refleja involuntaria rápida de los músculos de la cara y del miembro que sigue una progresión rostro-caudal (figura 2A). En algunas situaciones, la RS es solamente parcial. El músculo que responde más frecuentemente y con una latencia más corta es el orbicular de los párpados, seguido por el esternocleidomastoideo, el masetero y los músculos del tronco y de los miembros superiores e inferiores.

Aparte de las respuestas motores directas, un estímulo de sobresalto auditivo causa también cambios en la excitabilidad de estructuras a lo largo de la vía motora. A nivel cortical, Furubayashi et al. (2000) fueron los primeros en describir los efectos de un estímulo auditivo de alta intensidad en excitabilidad de la corteza motor. Estos autores demostraron que los estímulos auditivos de 80 DB inducen inhibición transitoria de los potenciales evocados motores estudiados por estimulación magnética transcraneal (EMT) sobre el área motor, pero ningún efecto se registró por estímulos eléctricos transcraneales. Tales resultados fueron confirmados posteriormente por Fisher et al. (2004), que examinó los efectos después de la habituación del ASR, para evitar interferencia con la respuesta a EMT. Kühn et al. (2004) demostraron que el efecto ocurre a nivel cortical, porque la inhibición fue observada solamente en potenciales evocados motores a EMT pero no en las respuestas motoras obtenidas por estímulo focal a través de los electrodos insertados en el núcleo subtalamico para tratamiento por estímulación cerebral profunda en pacientes con enfermedad de Parkinson. A nivel espinal, Delwaide et al. (1995) describieron una facilitación transitoria del reflejo H del músculo soleo después de un estímulo de sobresalto auditivo, sugiriendo que la activación del fascículo reticulospinal descendente causa un aumento de la excitabilidad de la motoneurona alfa a partir de un cierto tiempo después del estímulo.

1.3. Factores que influencian la magnitud de la reacción de sobresalto

La magnitud y la latencia de la RS varían entre individuos y también dependen de factores intraindividuales, es decir entre una prueba y otra. Los experimentos en animales demostraron que el tamaño de la RS auditiva era dependiente del ritmo circadiano, con un aumento del tamaño de la respuesta en la noche con respecto al día (Chabot y Taylor 1992), y del nivel de iluminación, con un aumento del tamaño de la respuesta relacionado con el aumento en intensidad de luz (Walker y Davis 1997). También, Paylor y Crawley (1997) han podido modificar genéticamente la expresión del RSA por medio de inducir más o menos IPP. En seres humanos, Kofler et al. (2001 a,b) examinó la influencia del sexo y la edad en la RS auditiva: En su estudio, las mujeres tenían una probabilidad más alta de RS, con respuestas más grandes que en los hombres. La excitabilidad de los circuitos del RS también es modulada por el humor, la atención, el miedo y otros estados emocionales (Ho et al. 1987; Liegeois-Chauvel et al. 1989; Lang et al. 1990; Grillon et al. 1991). Lang y Davis (2006) precisaron el paralelismo entre el tamaño de la RS y el nivel de alerta. El patrón de la RS auditiva se modifica según la postura (Brown et al. 1991b) y lateralidad (Kofler et al., 2008). Brown et al (1991b) encontraron que las respuestas de los músculos de la pierna tenían una latencia más corta y eran más frecuentes al estar en bipedestación que en sedestación. Kofler et al. (2008) encontraron respuestas de mayor amplitud en el esternocleidomastoideo contralateral, y en el bíceps braquial ipsilateral a la mano dominante que en los músculos correspondientes contralaterales. Todas estas observaciones reflejan la importancia de la organización del sistema motor básico de la RS en los actos motores de los seres humanos.

La RS auditiva es un reflejo polisináptico y debe tenerse en cuenta que, como en la mayoría de reflejos polisinápticos, la repetición del estímulo conduce a habituación de la respuesta. En el caso de la RS, es posible que la habituación se deba a depresión de la transmisión sináptica en la formación reticular pontina (Chokroverty et al. 1992). La habituación de la RS auditiva puede estar presente ya en la segunda vez que se presenta el mismo estímulo. Esto puede plantear algunos problemas en la evaluación neurofisiológica de la respuesta. Para evitar la habituación, algunos investigadores han propuesto aplicar los estímulos separados por un largo tiempo (Brown et al., 1991) y otros han propuesto aplicar estímulos auditivos de diversos tonos y frecuencias (Kofler et al., 2001a,b). Timman et al (1998) han propuesto la existencia de una relación directa entre la habituación de la RS y el aprendizaje no-asociativo. Estos autores demostraron que, con la presentación repetida de estímulos auditivos, la disminución del tamaño de la respuesta del músculo esternocleidomastoideo se correlacionó significativamente con la disminución del flujo cerebral regional sanguíneo en cerebelo intermedio. Por otro lado, el efecto StartReact comporta también una disminución de la habituación. Es decir, que cuando se aplica un estímulo auditivo en sujetos sanos preparados para reaccionar, la respuesta de sobresalto es más grande y se habitúa significativamente menos que en condiciones de no preparación motora (Valls-Solé et al., 1995, 1997).

1.4. Reacción sobresalto y inhibición prepulso (IPP)

Indudablemente, el aspecto más importante a considerar en la modulación de la RS es si hay un estímulo sensorial precediendo el estímulo sobresalto (prepulso) . El prepulso es cualquier estímulo de intensidad reducida, que no es capaz de causar una respuesta registrable por sí mismo pero induce cambios en la respuesta a un estímulo supraumbral subsiguiente (figura 5). Los efectos pueden ser facilitatorios o inhibitorios, dependiendo en parte del intervalo de tiempo entre el prepulso y el estímulo de sobresalto (Valls-Solé et al. 1999b). El efecto inhibitorio del prepulso (IPP) es el más conocido. Se puede obtener con estímulos de la misma o distinta modalidad sensorial que la que produce la RS (figura 6). El efecto inhibitorio del prepulso se conoce también con otros nombres: modificación refleja (Hoffman and Ison 1980; Ison and Hoffman 1983), anticipación del estímulo (Ison et al. 1990), y modulación sensitivomotora (Boulu et al. 1981; Swerdlow y Geyer 1993). La IPP no depende del aprendizaje ni de experiencias anteriores con estímulos similares. La IPP es probablemente consecuencia de focalizar la atención para procesar la información aportada por el prepulso (Graham 1975; Blumenthal y Gescheider 1987).

Representación esquemática del circuito del prepulso

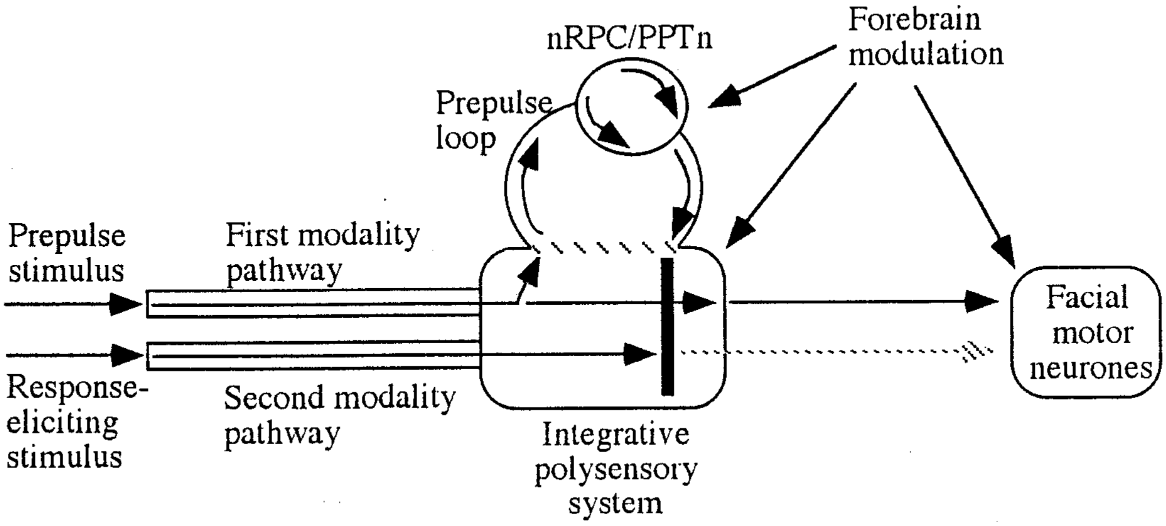


Figura 5. *El circuito esquemático propuesto para la inhibición por prepulso. El estímulo de prepulso es el primero que alcanza el tronco del cerebro a través de los circuitos usados por la modalidad sensorial utilizada. La descarga aferente incorpora dos circuitos distintos: el circuito que conduce a la activación de las motoneuronas faciales o de los extremidades (línea recta), y el circuito del prepulso, en el cual habrá algunos bucles que implican el núcleo reticular caudal de la protuberancia (nRPC) y el núcleo peduculopontine (PPN). Esto inducirá con una cierta demora la inhibición (línea gruesa vertical) que bloqueará la entrada de un nuevo impulso. Este circuito requiere un sistema polisensorial integrante de los impulsos de varias modalidades sensoriales, antes de la integración sensorimotor.*

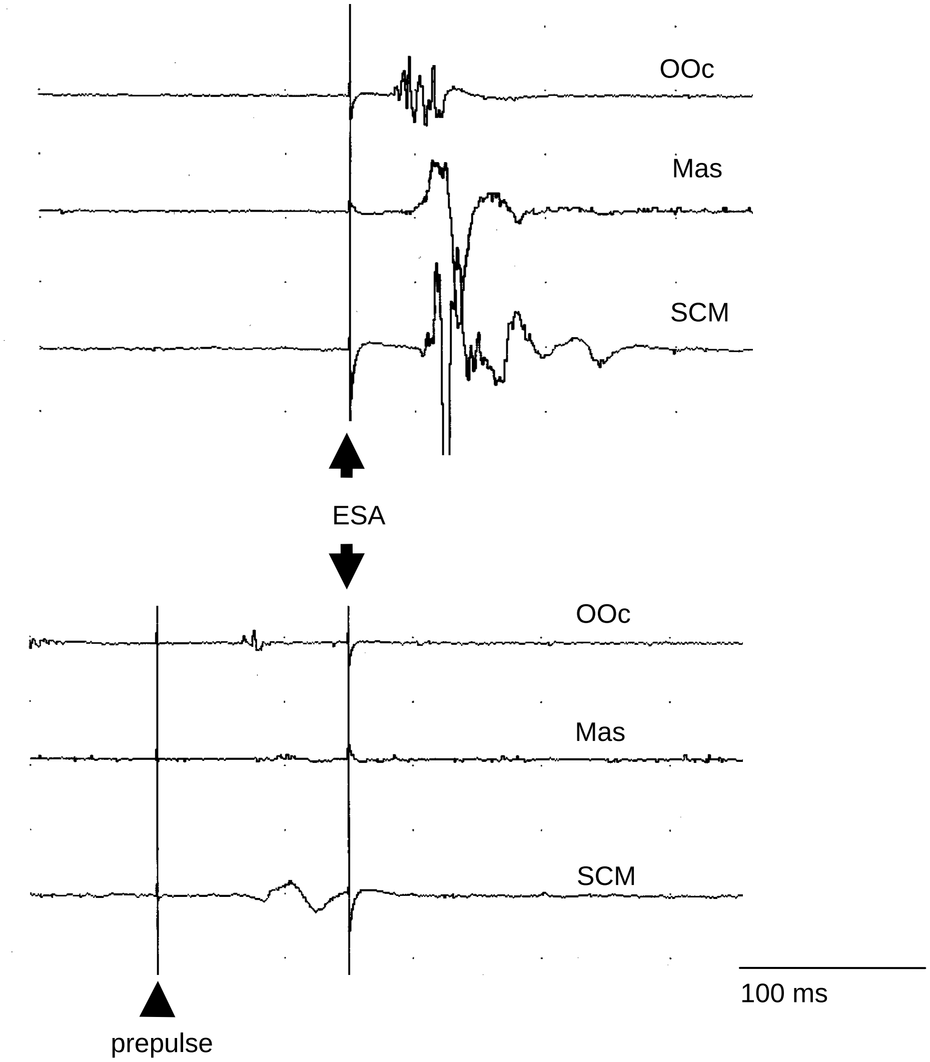


Figura 6. *Efecto de prepulso. Los trazos superiores corresponden a una reacción de sobresalto a un estímulo auditivo. Los trazos inferiores corresponden a un registro en el cual el estímulo auditivo se aplico 100ms después de un estimulo de prepulso somatosensorial, (estímulo eléctrico débil sobre el nervio digital del tercer dedo).*

1.5. Medida de la excitabilidad del circuito de sobresalto antes de la reacción voluntaria.

Los paradigmas del tiempo de reacción han sido ampliamente utilizados para medir la velocidad del procesamiento de la información en diversidad de tareas (Jahanshahi 2003). Los registros intracerebrales en monos han demostrado que la actividad neuronal en la corteza motora primaria, relacionada con el inicio del movimiento, aumenta aproximadamente en 60-100 ms antes de mover en respuesta a un estímulo externo (Evarts 1974). Las observaciones indirectas en seres humanos sugieren también que la excitabilidad de la corteza motora aumenta un poco antes de la ejecución del movimiento. Usando el estímulo eléctrico cortical en un paradigma de tiempo de reacción, Starr et al. (1988) observaron una disminución del umbral motor del músculo agonista. Con estímulo magnético transcranial (EMT), Pascual-Leone et al. (1992) mostraron que el tamaño del potencial evocado motor (PEM) aumenta progresivamente durante los 80ms precedentes al inicio de la actividad electromiográfica (EMG) en un movimiento balístico. Estas observaciones sugieren que la corteza motora es cada vez más excitable al acercarse el inicio del movimiento.

La ejecución de un movimiento balístico en un paradigma de tiempo de reacción se puede adelantar significativamente, si un estímulo de sobresalto auditivo (ESA) se aplica al mismo instante, o a un intervalo corto después de, la señal imperativa (Valls-Solé et al.. 1995, 1999; Siegmund et al. 2001;

Carlsen et al. 2003; 2004a, b). Este efecto del ESA sugiere que la excitabilidad del tracto reticuloespinal está aumentada durante la preparación para la ejecución de una tarea motora. Sin embargo, no sabemos si este aumento de excitabilidad ocurre en el tracto reticuloespinal de manera similar a como ocurre en la corteza motora en el curso de la preparación. Definir el curso del aumento de excitabilidad de la via retículoespinal es de interés fisiológico ya que si este aumento es paralelo con el de la corteza motora podría ser secundario a éste, mientras que si el curso del aumento de excitabilidad es diferente en ambos circuitos indicaría diferencias entre preparación y ejecución. La contestación a esta pregunta se buscó analizando el tamaño de las respuestas inducidas por un ESA aplicado en intervalos variables después de la señal imperativa en un experimento de tiempo de reacción simple (SRT).

1.6. Reacción de sobresalto en el contexto de movimientos voluntarios

Las reacciones voluntarias humanas más rápidas son las realizadas en el contexto de una tarea simple de tiempo de reacción, donde los sujetos son capaces de preparar suficientemente por adelantado sus programas motores para ejecución rápida al percibir la señal imperativa (“go”). Sin embargo, si la señal imperativa se acompaña de un estímulo de sobresalto inesperado, el tiempo de reacción llega a ser significativamente más corto que cuando reacciona a la presentación aislada de la señal imperativa (Valls-Sóle et al. 1995, 1999a; Siegmund et al.,. 2001; Carlsen et al., 2004a,b). En este efecto, denominado ‘StartReact’, el movimiento ejecutado es el que ha sido preparado. Esto fue demostrado por Castellote et al. (2007) que examinaron el StartReact con los movimientos sacádicos de los ojos. Estos autores mostraron que, después de que un StartReact modulara el movimiento sacádico, los ojos se direccionaban sobre la diana pre-establecida con la misma exactitud y precisión que cuando la sacada se ejecutaba en condiciones basales (no modulada por un efecto de StartReact).

El efecto de StartReact está convincentemente presente en tareas simples del tiempo de reacción. Está también presente con algunas reservas en tareas de tiempo de reacción de elección: Mientras que Carlsen et al. (2004a) presentaron evidencia de la ausencia del efecto en tareas de tiempo de reacción de elección cuando los errores fueron eliminados del análisis, Valls-Sóle (2004) encontró un efecto significativo de StartReact, si se incluían en el análisis los ensayos en los que el sujeto reaccionaba con la mano incorrecta en un porcentaje de casos. Esto significa que hay un cierto grado de preparación subcortical en paradigmas de tiempo de reacción de elección, que va posiblemente junto con un aumento general de la atención pre-movimiento y podría conducir al error característico de la precipitación en la ejecución de una tarea preparada, tal como se observa en un buen número de situaciones en las cuales hay apremios del tiempo, tales como en el caso del portero que intenta parar un penalti lanzándose precipitadamente hacia el lado incorrecto de la línea de gol antes de que la pelota haya comenzado a moverse.

El efecto StartReact podía teóricamente ser debido por lo menos a dos mecanismos posibles: Uno es que al aumentar la energía de la entrada sensorial se acelera el procesamiento sensitivomotor y todos los procesos sinápticos necesarios para la ejecución de la tarea. Este mecanismo se ha definido como facilitación intersensorial (Nickerson 1973; Gielen etal., 1983; Terao et al., 1997), un proceso por el cual la reacción a una señal sensorial se acorta cuando una señal de otra modalidad sensorial se aplica simultáneamente. La adición de un estímulo de sobresalto proporciona ciertamente un aumento significativo de energía a la señal imperativa y, por tanto, la facilitación intersensorial podría explicar un cierto efecto. Sin embargo, la cantidad de acortamiento de tiempo de reacción simple (SRT) debida a facilitación intersensorial es de alrededor de 50 ms (Nickerson, 1973), mientras que el acortamiento de SRT en el efecto de StartReact puede ser de más de 100ms. Realmente, en la mayoría de los casos, el tiempo de reacción en el paradigma de StartReact tiene valores similares a los de la latencia del RS (del orden de 70ms para los músculos del antebrazo). En este tiempo, la conexión sensitivomotora habría sido apenas posible a nivel cortical (Valls-Solé et al. 1999a). Por lo tanto se hace necesario considerar un segundo mecanismo, por el cual el estímulo de sobresalto activaría el conjunto de estructuras neuronales necesarias para la ejecución de la tarea a nivel subcortical, sin pasar por los procesos corticales de integración sensitivomotora (Valls-Solé et al. 1999; Sanegre et al. 2004; Carlsen et al. 2004a). Para ello, el programa motor debe ser representado en estructuras subcorticales motoras y mantenerse a punto de ser lanzado en el momento de la percepción del estímulo auditivo. El hecho de que los sujetos ejecutan la misma tarea sin distorsión sugiere que los comandos voluntarios viajan por los mismos circuitos activados en la RS (es decir, el tracto reticulospinal). Si los comandos voluntarios transitaran por el tracto corticospinal, se hubiera producido colisión entre los impulsos descendentes voluntarios y los involuntarios que descienden necesariamente por el tracto retículoespinal después de la aplicación de ESA y el programa motor se modificaría perceptiblemente. Por lo tanto, sin negar la posibilidad de una cierta contribución de la facilitación intersensorial, los experimentos descritos más abajo han proporcionado evidencia adicional en favor del papel de la formación reticular y el tracto reticuloespinal en la ejecución de movimientos balísticos voluntarios.

1.7. Tarea doble

La realización de una tarea unimanual cuando se efectúan simultáneamente movimientos voluntarios rítmicos con la mano contralateral es un paradigma útil para el estudio del efecto de interferencia de una tarea motora sobre otra (Pashler 1994; Herath et al. 2001). En tales condiciones típicamente se deteriora el funcionamiento de una de las acciones (Geurts et al. 1991; Lundin-Olsson et al. 1997; Mulder et al. 2002; Kumru et al. 2004; Jiang 2004). ¿Por qué es tan difícil hacer dos tareas motoras al mismo tiempo? Varios autores han sugerido la existencia de un cuello de botella en el procesamiento central de impulsos (Pashler, 1984, 1994; Pashler y

Johnston, 1998). En esta teoría, solo una tarea de entre varias superaría el proceso de selección y otras tareas quedarían relegadas de tal manera que recibirían menos atención. La selección de la tarea 2 no comenzaría hasta que se termina la selección de la tarea 1. Los mecanismos fisiológicos que permiten explicar la interferencia entre tareas no son totalmente conocidos. Ejecutar un plan motor puede implicar la generación de comandos inhibitorios para las estructuras motoras no implicadas en la acción voluntaria (Gerloff et al. 1998; Kumru et al. 2004; Gorsler et al. 2004). Si una de las acciones implica reaccionar a una señal sensorial, otros factores relacionados con el procesamiento en el sistema sensorial tienen que entrar en consideración, incluyendo la atención dividida (Sakai et al. 2000; Herath et al. 2001; Fernandes et al. 2006). Probablemente, muchos mecanismos contribuyen simultáneamente a la interferencia entre tareas. La relevancia de cada uno de estos factores puede variar dependiendo del paradigma experimental específico.

Los estudios que conforman el cuerpo de esta tesis han tenido como uno de sus objetivos el de entender mejor los mecanismos del control del motor al ejecutar movimientos balísticos y, entre ellos, conocer como interfiere la realización de un movimiento balístico con la ejecución de otra tarea.

Capitulo 2. – Justificación de los estudios

Las siguientes consideraciones constituyen la base de los argumentos usados en la construcción de la hipótesis de trabajo y de los objetivos de esta tesis.

2.1. Sobre la excitabilidad del circuito subcortical motor durante preparación motora. Los paradigmas del tiempo de reacción han sido ampliamente utilizados para medir la velocidad de procesamiento de la información en tareas diversas (Jahanshahi 2003). Los registros intracerebrales en monos han demostrado que la actividad neuronal de la corteza motora primaria relacionada con el inicio del movimiento aumenta aproximadamente 60-100 ms antes de la respuesta motora a un estímulo externo (Evarts 1974). Usando el estímulo eléctrico cortical dentro de un paradigma de tiempo de reacción, Starr et al. (1988) observó una disminución del umbral motor del músculo agonista precediendo al movimiento, sugiriendo que la corteza motora se hace progresivamente más excitable justo antes de iniciarse el movimiento. De manera similar, Pascual-Leone et al. (1992) usaron el estímulo magnético transcranial (EMT), para demostrar que el tamaño del potencial evocado motor (PEM) aumenta progresivamente durante los últimos 80 ms antes del inicio de la actividad electromiográfica en un movimiento balístico.

La ejecución de un movimiento balístico en un paradigma de tiempo de reacción se puede acelerar significativamente si un estímulo que causa sobresalto auditivo se aplica junto con la señal imperativa o en un corto intervalo de tiempo después de ella (Valls-Sóle et al. 1995, 1999; Siegmund et al. 2001; Carlsen et al. 2003; 2004a, b). Estos resultados sugieren un aumento de la excitabilidad de la formación reticular y del tracto reticuloespinal durante la preparación para la ejecución de una tarea motora. Sin embargo, no sabemos si la modificación de la excitabilidad del tracto reticuloespinal sigue o no el mismo perfil temporal que la de la corteza motora.

2.2. Sobre la sincronización de los cambios de la excitabilidad durante la ejecución de la tarea motora. Los músculos orbicularis oculi (OOc) y esternocleidomastoideo (SCM) son los músculos más constantemente activados en la RS a un estímulo auditivo (Brown et al. 1991a; Kofler et al. 2001b). En igualdad de otras condiciones, un cambio en el tamaño de la RS debería reflejar la excitabilidad de la via motora subcortical y, en determinadas condiciones experimentales, los efectos modulatorios de dicha condición experimental en la activación involuntaria del tracto subcortical motor. Este acercamiento se ha utilizado extensivamente en psicofisiología (Bradley et al. 2005). Por lo tanto, consideramos que el tamaño de la RS registrada en OOc y SCM reflejaría por lo menos en parte el nivel de la excitabilidad de los centros subcorticales motores. Debido a ello, analizamos si el tamaño de la reacción de sobresalto fue modificado en dos paradigmas experimentales bien escogidos: Tiempo de reacción de elección forzada (tREF), un paradigma en el cual el sujeto debía reaccionar sea con la mano derecha o sea con la mano izquierda, y paradigma de Go/noGo (GnG), en el que el sujeto debía reaccionar a determinados estímulos pero debía evitar la reacción en otros estímulos. Nuestra hipótesis fue que la excitabilidad de los centros subcorticales motores debería ser menor en el paradigma GnG que en el paradigma tREF al incluir la posibilidad de no reaccionar.

2.3. Sobre la inhibición por prepulso (IPP) durante la preparación motora. Una de las características de la RS es su susceptibilidad a ser inhibida por un estímulo sensorial débil precedente que no genere por si mismo ninguna respuesta refleja, un efecto conocido como inhibición por prepulso (Graham 1975; Blumenthal y Gescheider 1987; Ison et al., 1990; Swerdlow et al., 1995; Blumenthal 1999; Valls-Solé et al., 1999b). Aun cuando la relación entre el prepulso y la RS se ha estudiado a fondo en los sujetos sanos, siguen habiendo algunos puntos interesantes a explorar. Nuestra hipótesis fue que los efectos inhibitorios de prepulso sobre la RS podrían estar presentes durante la preparación motora y, por lo tanto, examinamos si la IPP de la RS estaría o no asociado con inhibición del efecto StartReact.

2.4. Efecto de StartReact en movimientos sacádicos de los ojos. Durante el parpadeo espontáneo, voluntario y reflejo o el cierre forzado del párpado, el globo ocular se retrae 1 o 2 milímetros debido a la co-contracción de todos los músculos extraoculares (Evinger et al., 1984; Collewijn et al., 1985; Bour et al., 2000). Un efecto similar se puede esperar en el parpadeo derivado de un ESA. Sin embargo, los efectos de un ESA en la preparación de las sacadas no son completamente claros. En particular, no se sabe si la aplicación de un ESA durante la preparación para la ejecución de un movimiento sacádico producirá un acortamiento de la latencia de los músculos extraoculares similar a la que se produce en los músculos de las extremidades (Valls-Solé et al. 1999; Carlsen et al. 2003, 2004). El nRPC desempeña un papel crucial en la generación de la RS (Leintner et al., 1980; Davis et al., 1982; Brown et al., 1991a). Las neuronas que descargan en fase premotora en relación con las sacadas horizontales en el hombre están en la parte intermedia del nRPC (Horn et al., 1995). El coliculo superior (CS) tiene conexiones bien conocidas con el nRPC (Isa y Naito 1995; Zhao y Davis 2004). Por lo tanto, nuestra hipótesis es que el efecto StartReact puede también observarse en los movimientos sacádicos.

2.5. Doble tarea. Es difícil que los seres humanos no entrenados mantengan el ritmo de un movimiento oscilatorio unilateral durante la ejecución de una acción voluntaria balística contralateral (Kumru et al., 2004). Esto se ha atribuido a que el programa motor para la realización de movimientos balísticos contiene comandos inhibitorios dirigidos a los músculos no implicados en el movimiento balístico, pero la fisiología exacta subyacente de este efecto no está totalmente clara. Por ello, la hipótesis considerada en este trabajo es doble: 1. Si el efecto es bidireccional, el mantenimiento de un movimiento oscilatorio con una mano deteriorará de alguna manera la reacción a ejecutar con la otra mano, y 2. Si la causa de tal deterioro funcional es una preparación defectuosa del circuito motor subcortical (es decir, la estructura subcortical motora no puede alcanzar el grado requerido de preparación para la ejecución rápida de un movimiento balístico), la interferencia en la doble tarea se mantendrá aun en condiciones en las que se de el efecto StartReact.

Capitulo 3. - Hipótesis

La hipótesis principal de este proyecto es que los circuitos que vehiculan la reacción de sobresalto participan en la ejecución de movimientos voluntarios balísticos en el ser humano. La ejecución rápida de un movimiento comporta una preparación motora que implica principalmente un aumento de excitabilidad en las estructuras que van a ser activadas a lo largo de la vía motora. Debido a dicho aumento de excitabilidad, impulsos que activen estructuras subcorticales con suficiente representación en el programa motor preparado pueden desencadenar la ejecución del movimiento sin necesidad de la participación de áreas motoras superiores.

Esta hipótesis general se subdivide en varias hipótesis parciales, que se especifican a continuación:

3.1. El circuito de la RS participa en la ejecución de movimientos voluntarios. Por lo tanto, la hipótesis de trabajo es que la excitabilidad del RS debería experimentar cambios temporales similares a los descritos para la excitabilidad de la vía córtico-espinal en el inicio del movimiento.

3.2. El circuito de la RS contribuye a la preparación motora para la ejecución de movimientos balísticos. Por lo tanto, la hipótesis de trabajo es que su excitabilidad debería cambiar de acuerdo a la instrucción y al tipo de reacción.

3.3. El efecto StartReact se debe a la participación de la vía del RS en la ejecución de movimientos balísticos y no a la adición simple de los comandos del movimiento voluntario a la RS. Por lo tanto, la hipótesis de trabajo es que el acortamiento del tiempo de reacción podría estar presente incluso cuando la RS está inhibida por la presencia de un estímulo de prepulso.

3.4. El movimiento realizado en la condición StartReact es igual de preciso que el movimiento balístico realizado voluntariamente. Por lo tanto, la hipótesis de trabajo es que la aceleración de movimientos sacádicos mediante el fenómeno StartReact no debería suponer ningún cambio significativo en el tiempo de reacción a un estímulo imperativo presentado en la diana visual.

3.5. El fenómeno StartReact refleja el grado de preparación motora subcortical. Por lo tanto, la hipótesis de trabajo es que el porcentaje de acortamiento en el tiempo de reacción debería disminuir en condiciones en las que se limita el grado de dicha preparación, tal como ocurre cuando el sistema motor está ocupado en la realización de un movimiento continúo.

Capitulo 4.- Objetivos

4.1. Estudiar el perfil temporal de los cambios de excitabilidad que ocurren en el circuito de la RS antes de la ejecución de una tarea motora.

4.2. Analizar si el cambio de excitabilidad pre-movimiento en el circuito de sobresalto se modifica en relación con el tipo de tarea motora en preparación.

4.3. Examinar si la inhibición por prepulso de la RS causa también inhibición del efecto StartReact en el contexto de una tarea simple de tiempo de reacción.

4.4. Determinar si el efecto StartReact se observa en los movimientos sacádicos horizontales del ojo y si dicho efecto implica un movimiento de fijación de la mirada con la misma exactitud que el movimiento voluntario en sí mismo.

4.5. Evaluar si el retraso en el tiempo de reacción unilateral que ocurre cuando se realiza un movimiento rítmico oscilatorio con el brazo contralateral (efecto de la tarea-doble) se relaciona con una disminución en la excitabilidad del circuito de sobresalto.

Capítulo 5. – Material y métodos

5.1. Instrucciones y registros

Se utilizaron electrodos de superficie de cloruro de plata para registrar la actividad EMG del músculo orbicularis oculi derecho (OOc), esternocleidomastoideo (SCM) y flexores y extensores de la muñeca (WF y WE).

La actividad EMG fue amplificada mediante un electromiógrafo convencional (Mystro5Plus electromyograph; Oxford Instruments, Surrey, UK). Los filtros usados para el registro fueron entre 50 y 1000 Hz. También se utilizó un acelerómetro para registro del movimiento con un filtro de frecuencias de 0.1 a 10 Hz. Todos los registros EMG y acelerométricos fueron grabados en papel termosensible para su análisis posterior.

5.2. Estímulo de sobresalto auditivo (ESA) y tiempo de reacción

El estímulo de sobresalto auditivo (ESA) fue un sonido de alta intensidad, capaz de producir una reacción de sobresalto. Se obtuvo descargando la bobina redonda de un estimulador magnético al 100% de intensidad sobre una plataforma metálica. El sonido producido mediante este método es de una intensidad de 130 DB (SPL), medida a una distancia de 1 m desde su origen, con un aparato Bruel - Kjaer Impulse Precision Sound Level Meter type 2204 (Valls-Solé et al., 1999).

5.2.1. Tiempo de reacción simple: Se presentó una señal que consistía en una cruz blanca presentada en el centro del monitor de un ordenador. Esto sirvió como señal imperativa para que el sujeto voluntario realizara el movimiento solicitado. Se pidió a los sujetos que prestaran atención a la pantalla, y estuvieran preparados para realizar una flexión rápida de la muñeca al aparecer la señal imperativa. Esta aparecía después de un anteperiodo fijo de 1000 ms. También se comunicó a los sujetos que podrían haber estímulos auditivos de alta intensidad durante el experimento, pero se les recordó que reaccionaran a la señal imperativa sin tener en cuenta la posible interferencia de otro estímulo.

Los intervalos entre IS y ESA fueron 0, 20, 40, 60, 80, y 100 ms. Se repitieron 5 ensayos para cada intervalo, mezclados aleatoriamente con un número significativamente mayor de ensayos sin ESA (ensayos control). Se realizaron 30 ensayos con ESA (5 para cada condición) y 70 ensayos control en cada sujeto. El ESA fue aplicado sin señal imperativa en 5 ensayos en cada sujeto (ensayos base) mezclados entre los ensayos de la prueba.

5.2.*2. Tiempo de reacción de elección forzada (tREF) y Go/noGo:*

Se solicitó a los sujetos que reaccionaran a una señal visual que aparecía en el monitor del ordenador. Después de una cruz blanca de 1×1 cm como una señal de aviso, la señal imperativa (cuadrado de 5×5 cm) apareció después de un anteperiodo fijo de 2000 ms en el lado derecho o izquierdo de la pantalla, a una distancia de 5 cm del punto central de fijación. En algunos ensayos presentados al azar (véase más abajo), la presentación de la señal imperativa fue acompañada de un estímulo auditivo de alta intensidad, capaz de producir una RS. El procedimiento experimental implicó dos sesiones separadas (para condición tREF y GNG, respectivamente), con un descanso corto entre ellas.

5.2.2.1. Tiempo de reacción de elección forzada (tREF) En esta sesión, se solicitó a los sujetos que realizaran una flexión rápida de la muñeca a la percepción de la señal imperativa (IS). Debían reaccionar con la mano derecha si aparecía la señal en el lado derecho de la pantalla y con la mano izquierda si la señal aparecía en el lado izquierdo de la pantalla.

5.2.2.2. Tarea Go/noGo (GnG): Este experimento fue subdividido en dos partes (GnG a la derecha y GnG a la izquierda). Los sujetos tenían la instrucción de realizar una flexión rápida de la muñeca con la mano que coincidía con el lado en el que aparecía la señal y no reaccionar si la señal aparecía en el lado contralateral.

En cada sesión, los experimentos fueron conducidos usando tres diversos tipos de ensayos: 1) ensayos control en los que solo se presentaba la señal imperativa. 2) Ensayos basal en los que solo se presentaba el ESA sin instrucción previa. 3) Ensayos prueba en los que el ESA fue presentado junto con la señal imperativa. En ensayos control y prueba, medimos la latencia del inicio de la actividad EMG registrada en los flexores de la muñeca (wrist flexor=WF) (LatWF) desde la señal imperativa. En ensayos prueba y basales, determinamos la latencia del inicio de la respuesta en OOc y SCM (LatOOc, LatSCM). También medimos el área de la actividad EMG del OOc y del SCM. También calculamos el número de respuestas correctas, expresado como el número medio de ensayos en los cuales el sujeto realizó la tarea correcta en porcentaje del número total de ensayos, para cada sesión.

5.2.3. Prepulso en el fenómeno StartReact: Los sujetos se sentaron en una silla enfrente de una pantalla de ordenador con sus manos y antebrazos en reposo encima de una mesa pequeña donde había también un interruptor montado en un soporte de madera. Tenían la instrucción de presionar el interruptor al percibir la señal imperativa visual. En algunos ensayos se aplicó junto con la señal imperativa el sonido de alta intensidad capaz de generar una RS y el efecto StartReact. En otros ensayos se presentó también un estímulo de prepulso somatosensorial, que consistió en un estímulo eléctrico de baja intensidad aplicado en el dedo índice. Los sujetos no sabían que tipo de ensayo se presentaba. No sabían si la señal imperativa iría acompañada o no del estímulo sonoro de alta intensidad o si habría o no un estímulo de prepulso. En total, utilizamos 7 condiciones distintas: **Reac** (solamente se presentaba la señal imperativa); **StartReact** (se presentaba un sonido de alta intensidad junto con la señal imperativa para producir el efecto StartReact); **PrepReact** (se presentaba el estímulo de prepulso en el dedo 100 ms antes de la señal imperativa); **PrepStartReact** (se presentaba la señal imperativa y el estímulo sonoro, precedidos 100 ms antes por el estímulo de prepulso); **Prep** (se presentaba solamente el estímulo eléctrico en el dedo sin señal imperativa ni instrucción previa); **Start** (se presentaba el sonido de alta intensidad sin ninguna instrucción para reaccionar ni señal imperativa) y **PrepStart** (se presentaba el estímulo de prepulso en el dedo 100ms antes del sonido de alta intensidad, sin presencia de ninguna señal imperativa ni instrucción para reaccionar).

5.2.4. ***Movimientos voluntarios saccadicos de los ojos y reacción de sobresalto:*** Los movimientos verticales y horizontales del ojo fueron registrados mediante electrodos de superficie para Electro-oculografia (EOG), colocados en los cuatro puntos de la órbita derecha (Heide et al. 1999). El electrodo activo para los movimientos verticales se colocó en el borde orbital inferior, mientras que el electrodo activo para los movimientos horizontales fue colocado en el borde orbital externo. También registramos la actividad del EMG de los músculos esternocleidomastoideo (SCM) mediante electrodos superficiales colocados sobre el vientre muscular. El antebrazo y la mano se colocaron sobre dos plataformas metálicas unidas por un gozne. Mediante dicha estructura se limitaron los movimientos de la extremidad, permitiendo solamente un movimiento de flexo-extensión de la muñeca. Al sistema se acopló un potenciómetro justo en el punto de rotación de las dos plataformas a fin de registrar el movimiento. Todas las señales bioeléctricas fueron registradas y almacenadas temporalmente mediante un electromiógrafo convencional (MYSTRO5Plus; Oxford Medical Instruments, Surrey, UK). Los filtros de frecuencia para los movimientos del ojo y de la mano fueron 0.1-20 Hz, mientras que el EMG del SCM fue registrado con una banda de frecuencias de 50 a 1000 Hz. El movimiento del ojo hacia el electrodo activo y el movimiento de flexión de la muñeca fueron representados como desviaciones negativas a partir de la línea de base**.** Un círculo de 2 cm de diámetro colocado enfrente del sujeto sirvió como punto de fijación de la mirada. Se instaló un monitor de ordenador en el campo visual derecho del sujeto, donde se proyectó el estímulo visual, consistente en un cuadrado de 5 cm^2 de color blanco en fondo gris. Esta diana se generaba cuando uno de los experimentadores presionaba una tecla del ordenador. Se presentaba siempre en el mismo punto, a una distancia angular de 15° a la derecha del punto de la fijación de la mirada fija. La propia diana congenia una señal imperativa, a la que los sujetos debían reaccionar. Esta consistía en una flecha apuntando a la derecha o a la izquierda. Los sujetos debían reaccionar con su mano derecha a la instrucción que contenía la diana visual (flexión si la flecha apuntaba hacia la izquierda y extensión si la flecha apuntaba hacia la derecha. La distribución de señales imperativas apuntando hacia la derecha o izquierda fue randomizada, con un 40% para cada lado y el 20% de ensayos restantes en los que en vez de triángulo aparecía un cuadrado, indicando que no debían efectuar ningún movimiento.

Los sujetos tenían la instrucción de realizar un movimiento rápido del ojo desde el punto de fijación de la mirada hasta la diana (15°) En todos los casos, el punto inicial de la fijación de la mirada fija seguía estando presente. También se pidió a los sujetos que estuvieran preparados para reaccionar realizando una flexión o extensión rápidas de la muñeca al percibir el símbolo incluido en la diana. Como en otras pruebas, se advirtió a nuestros sujetos de la posibilidad de que un ESA podría estar presente en algunos de los ensayos, y se les animó a que se prepararan para reaccionar a la señal visual sin tener en cuenta la posible interferencia de estímulos acústicos. No se dieron otras instrucciones en ensayos de control. En los ensayos prueba, entremezclados aleatoriamente con los ensayos control, la presentación de la diana fue acompañada del ESA. Para mantener la atención del sujeto, el ESA fue aplicado por sí solo en tres ensayos entremezclados entre ensayos control y prueba. En los ensayos en los que el ESA fue aplicado solo no se presentó el ningún aviso verbal o señal visual. Ensayos en los cuales los sujetos comenzaron un movimiento del ojo durante un período de 1 s antes de la presentación de la diana fueron excluidos. También excluimos los ensayos en los cuales los sujetos hicieron un movimiento precipitado de la mano (antes del final del movimiento sacádico del ojo) o movieron la mano en la dirección incorrecta. En estos casos, los ensayos fueron contados como errores y se repitió el ensayo. El experimento terminó con un total de 50 ensayos por cada sujeto, que incluían 40 ensayos control y diez ensayos prueba para cada condición. La señal imperativa que formaba parte de la diana visual requería la flexión o la extensión de la muñeca fue presentada en 20 ensayos cada uno, mientras que en los diez ensayos restantes, los sujetos no debían reaccionar.

5.2.5. Para la tarea doble*:* El procedimiento implicó dos condiciones experimentales: **A)** En la condición control, los sujetos habían recibido ya la instrucción de mantener sus manos encima de la mesa, en reposo, hasta que realizaran la reacción simple (SRT). **B)**. En la condición prueba, los sujetos tenían que realizar los movimientos oscilatorios unilaterales rítmicos de la muñeca tipo temblor y realizar la misma tarea como se describe anteriormente con la mano contralateral. No especificamos frecuencia o amplitud del movimiento oscilatorio. El movimiento oscilatorio debía ser constante y rítmico, cómodo y que se pudiera mantener durante el tiempo necesario.

Capitulo 6.- Análisis estadístico

Todas las variables fueron recogidas en una base de datos (Microsoft Excel).

Los estudios estadísticos se realizaron con el programa estadístico SSPS 11 o 13, aplicando básicamente las siguientes pruebas:

1. Para el estudio de distribución de datos: prueba de Kolmogorov-Smirnov
2. Para la comparación de variables cuantitativas:
    a) Variables paramétricas:
        - Prueba T de Student para comparación de medias
        - ANOVA para el análisis de varianzas, con corrección de Bonferroni para comparaciones múltiples

    b) Variables no paramétricas:
        - Prueba de Wilcoxon para datos apareados
        - Pruebas U de Mann-Whitney para datos no apareados
3. Pruebas de correlación simple:
    a) Variables paramétricas:
        - Prueba de Pearson

    b) Variables no paramétricas:
        - Prueba de Spearman

Capitulo 7.- Resultados y publicaciones en las que se basa el presente trabajo de tesis

7.1. Los resultados del estudio que hacen referencia al objetivo (4.1) se presentan en el trabajo:

"*Excitability of the pathways mediating the startle reaction before execution of a voluntary movement*". Experimental Brain Research 2006;169:427-432.

7.2. Los resultados del estudio que hacen referencia al objetivo (4.2) se presentan en el trabajo:

"*Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks*". Neuroscience Letters. 2006;406:66-70.

7.3. Los resultados del estudio que hacen referencia al objetivo (4.3) se presentan en el trabajo:

"*The effects of a prepulse on the startreact phenomenon*". Suppl Clin Neurophysiol. 2006; 58: 101-9.

7.4. Los resultados del estudio que hacen referencia al objetivo (4.4) se presentan en el trabajo:

”*Voluntary saccadic movements speeded up by a startle*”. Experimental Brain Research. 2007; 177: 129-36.

7.5. Los resultados del estudio que hacen referencia al objetivo (4.5) se presentan en el trabajo:

”*Unilateral reaction time task is delayed during contralateral movements*”. Experimental Brain Research. 2007;181:469-75.

I. PUBLICACIÓN

Excitability of the pathways mediating the startle reaction before execution of a voluntary movement.

Experimental Brain Research 2006;169:427-432.

7.1. La preparación para la ejecución de una acción implica el aumento de actividad a nivel subcortical.

El ESA proporcionó la energía requerida por el sistema para ejecutar el programa motor entero antes de que llegue a tener efecto el comando voluntario. Al realizar un movimiento balístico voluntariamente, este último paso en el aumento de la excitabilidad de los circuitos motores se genera a nivel cortical y se transmite hacia zonas cortico-subcorticales. El aumento en la excitabilidad de la vía corticospinal, que ocurre 60-100 ms antes del inicio de la actividad del EMG, serviría como el disparador para el movimiento previsto, preparado convenientemente y guardado para su ejecución, a nivel subcortical.

Exp Brain Res (2006) 169: 427–432
DOI 10.1007/s00221-005-0156-1

RESEARCH ARTICLE

Hatice Kumru · Josep Valls-Solé

Excitability of the pathways mediating the startle reaction before execution of a voluntary movement

Received: 28 June 2005 / Accepted: 30 July 2005 / Published online: 5 November 2005

Abstract Studies with transcranial electrical or magnetic stimulation have shown a progressive increase of motor cortex excitability beginning at about 80 ms before the onset of electromyographic (EMG) activity in a voluntary movement. We studied whether a similar increase in excitability occurs in subcortical motor tracts before execution of a ballistic movement. In ten healthy volunteers, we examined the effects of a startling auditory stimulus (SAS) applied at various intervals following the imperative signal (IS) in a reaction time task experiment. We hypothesized that, if the excitability of the reticulospinal tract increases before onset of muscle activity, there would be a corresponding change in the size of the startle response elicited either in muscles responding to the SAS, the orbicularis oculi (OOc) and sternocleidomastoid (SCM), or in the agonist muscle for the reaction. A SAS was applied at intervals of 0, 20, 40, 60, 80, and 100 ms after IS in a reaction time task paradigm in which subjects had to perform a ballistic movement of wrist flexion. We measured the size of the EMG bursts recorded in the OOc and the SCM, as well as the size of the first EMG burst in the wrist flexors (WF). Comparisons were done with data obtained in baseline trials, in which unexpected SAS of the same intensity were delivered without preparation, and control trials, in which subjects performed the same motor task with no SAS. The size of the averaged OOc, SCM, and WF were larger in trials with SAS than in baseline or control trials, with significant differences in the SCM and in the WF ($p < 0.05$). However, there were no effects of time interval on the size of OOc, SCM, or WF ($p > 0.05$). These results indicate that, in the execution of a ballistic movement, the excitability of the subcortical motor tracts activated by a SAS is similarly enhanced at the time of the IS and 100 ms afterwards, just before the onset of EMG activity. We conclude that, in contrast with the reported progressive increase of excitability in the corticospinal tract, the excitability of the tracts activated by a SAS do not change between the IS and the onset of EMG activity.

Introduction

Reaction time paradigms have been widely used to measure the speed of information processing in a diversity of tasks (Jahanshahi 2003). Intracerebral recordings in monkeys have shown that the movement onset-related neuronal activity of the primary motor cortex increases at approximately 60–100 ms before moving in response to an external stimulus (Evarts 1974). Indirect observations in humans suggest also that the excitability of the motor cortex increases just before movement execution. Using cortical electrical stimulation within a reaction time task paradigm, Starr et al. (1988) observed a pre-movement decrease of motor threshold in the agonist muscle. With transcranial magnetic stimulation (TMS), Pascual-Leone et al. (1992) demonstrated that the size of the motor evoked potential (MEP) increased progressively during the last 80 ms before the onset of electromyographic (EMG) activity in a ballistic movement. These observations suggest that the motor cortex becomes increasingly excitable just before movement onset.

The execution of a ballistic movement in a reaction time task paradigm can be speeded up significantly if a startling acoustic stimulus (SAS) is applied together with the imperative signal or at a short interval afterwards (Valls-Sole et al. 1995, 1999; Siegmund et al. 2001; Carlsen et al. 2003; 2004a, b). These findings suggest an

H. Kumru
Unitat d'EMG, Servei de Neurologia, Facultad de Medicina, Universitat de Barcelona, Institut d'Investigació Biomèdica August Pi i Sunyer (IDIBAPS), Barcelona, Spain

J. Valls-Solé (✉)
Servei de Neurologia, Hospital Clínic, Unitat d'EMG, Villarroel 170, 08036 Barcelona, Spain
E-mail: jvalls@clinic.ub.es
Tel.: +34-932275413
Fax: +34-932275783

enhancement of excitability of the reticulospinal tract during motor preparation for the execution of a motor task. However, we do not know whether the excitability of the reticulospinal tract changes in a way similar to that of the motor cortex before execution of a motor task. In the study presented here, we analyzed the size of the responses induced by a SAS when the stimuli were applied at varying intervals after the imperative signal in a simple reaction time (SRT) experiment.

Subjects and methods

Ten healthy right-handed volunteers (seven men, three women, aged between 25 and 53 years) were studied. All gave written informed consent for the study, which was approved by our local Ethics committee.

Subjects were seated on a chair with padded armrests, facing a table with a computer screen at approximately 50 cm from their eyes. The subject's forearm and hand were firmly attached to two joined metallic platforms in such a way that the wrist had only one degree of freedom for flexo-extension movements. A potentiometer, built in the hinge joining forearm and hand platforms, was used to record the wrist joint position signal and calculate the time-dependent kinematic variables. Silver–silver chloride surface electrodes were used to record the EMG activity of the right orbicularis oculi (OOc), sternocleidomastoid (SCM), wrist flexors (WF), and wrist extensor (WE) muscles.

The EMG activity was amplified using a conventional EMG machine (Mystro5Plus electromyograph; Oxford Instruments, Surrey, UK) with band pass frequency filters between 50 and 1,000 Hz. All EMG and movement signal recordings were printed on thermosensitive paper for off-line analysis.

Auditory stimuli

The auditory stimulus (SAS) was a loud sound, capable of producing a startle reaction, obtained by discharging the magnetic coil from a magnetic stimulator over a metallic platform. The sound produced in this way is of an intensity of 130 dB sound pressure level (SPL), measured at a distance of 1 m from the source with a Brüel and Kjaer Impulse Precision Sound Level Meter type 2204 (Valls-Solé et al. 1999).

Experimental procedure

Subjects received full verbal instructions on the general experimental procedure. A signal consisting of a white cross was made to appear in the center of the computer monitor, which served as a warning signal for an incoming trial. Subjects were told to pay attention to the screen, and be prepared to perform a rapid flexion of the wrist at the perception of the imperative signal (IS), which appeared after a fixed foreperiod of 1,000 ms. Subjects were given a few trials of practice to feel comfortable with the task. Also, they were warned that there could be loud auditory stimuli presented during the experiment, but were encouraged to react to the IS regardless of any interference. The actual time intervals between IS and SAS were 0, 20, 40, 60, 80, and 100 ms. Five trials were repeated for each interval, intermingled randomly with a significantly larger number of trials with no SAS (control trials). We ended up with 30 test trials (five for each condition) and 70 control trials for each subject. Also, SAS was applied without IS in five trials in each subject (baseline trials) intermingled among the test trials.

Data analysis

Reaction time was determined by measuring the onset latency of the EMG signal in the WF (LatWF) from the IS in control and test trials. We also recorded the movement signal and the pattern of the EMG bursts in the agonist and the antagonist muscles, but these parameters were not further analyzed. Size of the EMG burst in the agonist muscle (SizeWF) was calculated by multiplying peak-to-peak amplitude times duration. LatWF and SizeWF measured in control trials were used as the reference values for the same data obtained in test trials. In trials containing SAS, we determined the onset latency and size of the burst of EMG activity recorded in the OOc and the SCM. Onset latency (LatOOc and LatSCM) was determined from the SAS. Size of the EMG burst (SizeOOc and SizeSCM) was again calculated by multiplying peak-to-peak amplitude times duration. The mean size of the startle reaction calculated in baseline trials was used as the individual's reference value for normalization of data.

All data were grouped according to the following conditions: baseline trials, control trials, and test trials (SAS-0, SAS-20, SAS-40, SAS-60, SAS-80, and SAS-100). The mean and standard deviation were calculated for each subject for data grouped according to the interval from the IS. For SizeOOc and SizeSCM, we calculated the grand mean out of the individual's percentages obtained for each interval from the corresponding data in baseline trials. For SizeWF, the grand mean was calculated out of the individual's percentages obtained from the corresponding data in control trials.

Statistical analyses were done with one-way ANOVA for comparison of all parameters regarding latency and size in all muscles for all conditions. To examine whether the variable time interval had any effect on reaction time or on the size of the responses, we performed statistical comparison of data grouped on intervals within each condition, using repeated measures of ANOVA. For reaction time and SizeWF, comparisons were made between the control condition and the six test conditions. For size of the startle reaction, comparisons were made between the baseline startle reaction and the six test conditions. Post hoc comparisons were made using Bonferroni's test. The statistical significant level was set at $p < 0.05$.

Results

All subjects completed the experiments without any difficulty. As expected, startle-related bursts of activity were present in the OOc and in the SCM in trials containing SAS (both, baseline and tests), while there were no time-locked bursts of EMG activity in OOc or SCM in any of the control trials. Responses induced by SAS in baseline trials showed interindividual differences in the latency and size of the initial response and in the degree of habituation with stimulus repetition. In all subjects, however, the responses observed in the fifth baseline trial were smaller than the responses observed in the first baseline trial. Habituation was noticeably larger in the SCM (from 4,630 μVs·ms as the mean response to the first stimulus to 975 μVs·ms as a mean response to the fifth stimulus) than in the OOc (from 6,196 μVs·ms as a mean response to the first stimulus to 5,125 μVs·ms as a mean response to the fifth stimulus). The absolute values of the mean startle response obtained by averaging together the responses to the five baseline trials was 2,411.0 μVs·ms (SD = 1,573.6 μVs·ms) for the OOc, and 5,646.2 μVs·ms (SD = 441.4 μVs·ms) for the SCM.

The EMG activity was configured in a characteristic three-burst pattern (Hallett et al. 1975). The first burst of the agonist muscle was followed by a burst in the antagonist muscle and a second burst in the agonist muscle. The three-burst EMG pattern, and the signal from the movement transducer, followed the changes in LatWF in such a way that there were no visually noticeable differences between control and test trials. The inter-bursts relationship of the three bursts EMG pattern, an aspect fully analyzed in previous works (Valls-Solé et al. 1999; Castellote et al. 2004), was not measured here. Figure 1 shows representative examples of a control trial (a), a baseline trial (b), and two test trials (c and d) at different time intervals. Note that the changes in reaction time do not modify substantially the shape of the three-bursts pattern nor the relationship between the bursts of EMG activity and the movement signal.

Reaction time

The grand mean of LatWF (considering all subjects together) was 201 ± 21 ms for the condition control, and 101 ± 32 ms for the condition SAS-0 (Table 1). In test trials with increasingly longer intervals, reaction time was progressively longer. The one-way ANOVA showed statistically significant effects of time interval on LatWF ($F_{(6,63)} = 27.9$; $p < 0.0001$). Post hoc analysis showed that differences were present between control trials and each SAS condition ($p = 0.01$), except for SAS-100 ms, in which the differences were not significant ($p > 0.05$).

Latency of the startle reaction

The grand mean latency for OOc and SCM was not different for baseline and test trials (Table 1). Statistical analysis showed no significant effects of time interval on

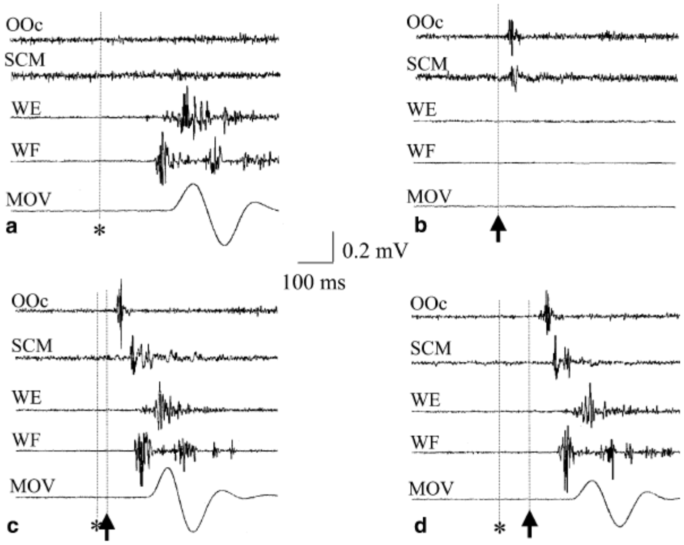


Fig. 1 Examples of recordings from a representative subject. Traces from top to bottom in each graph are the EMG activity from orbicularis oculi (*OOc*), sternocleidomastoid (*SCM*), wrist extensors (*WE*), and wrist flexor (*WF*) muscles, and the movement transducer signal (*MOV*). **a** Control trial, in which the subject had to respond to the imperative signal (*IS*); **b** baseline trial, in which the subject received an unexpected loud startling acoustic stimulus (*SAS*); **c**, **d** test trials with intervals between IS and SAS of 20 and 80 ms respectively

Table 1 Mean latencies of the EMG activity recorded in wrist flexor muscles in control trials, and in the orbicularis oculi and sternocleidomastoid muscles in baseline trials, and of all of them from test trials

	Baseline trials	Control trials	Test trials					
			0	20	40	60	80	100
Wrist flexors		201 (21)	101 (32)	119 (23)	129 (22)	150 (15)	165 (16)	188 (20)
Orbicularis oculi	40 (5)		39 (3)	39 (7)	41 (10)	39 (9)	44 (9)	38 (7)
Sternocleidomastoid	78 (29)		78 (28)	75 (28)	66 (31)	71 (35)	69 (40)	68 (27)

Data, in milliseconds, are the mean latency and one standard deviation (within *parenthesis*). Latency for the wrist flexors was calculated from IS. Latency for the orbicularis oculi and sternocleidomastoid muscles was calculated from SAS

Control trials are those in which subjects had to react to the presentation of an imperative signal. Baseline trials are those in which we applied the startling auditory stimulus with no motor preparation. Test trials are those in which the startling auditory stimulus was delivered, at the interval marked in milliseconds in each column, after the imperative signal

LatOOc ($F_{(6,63)} = 1.2$; $p = 0.3$) or on LatSCM ($F_{(6,63)} = 0.4$; $p = 0.8$).

Size of the first agonist burst of EMG activity in the wrist flexors

Figure 2 shows data on SizeWF in control and test trials. The statistical analysis indicated significant differences between conditions ($F_{(6,63)} = 3.2$; $p = 0.008$). Post hoc analysis showed that SizeWF was larger in test trials than in control trials ($p < 0.05$). However, time intervals did not have any significant effect on SizeWF ($p > 0.05$).

Size of the startle reaction

SizeOOc and SizeSCM were larger in test trials than in baseline trials (Fig. 2). Statistical comparison showed significant differences in SizeSCM ($F_{(6,63)} = 4.6$; $p = 0.001$), but differences in SizeOOc did not reach statistical significance ($F_{(6,63)} = 1.7$; $p = 0.1$). There were no differences in SizeSCM between trials of the test conditions.

Discussion

In the present study, we used the startle reaction as a probe to determine whether the subcortical motor pathways activated by a SAS undergo any change in excitability during the time immediately before execution of a voluntary ballistic movement. Our results indicate that, while SAS induced a larger response before execution of ballistic movement in comparison to rest, the size of the responses induced by the same intensity SAS did not change during the 100 ms preceding onset of voluntary movement. Other observations of interest are that the first EMG burst of the agonist muscle was of a similar size in all test trials, with no time interval-dependent changes, and that the latency of the startle response (LatOOc and LatSCM) was not different in test and baseline conditions.

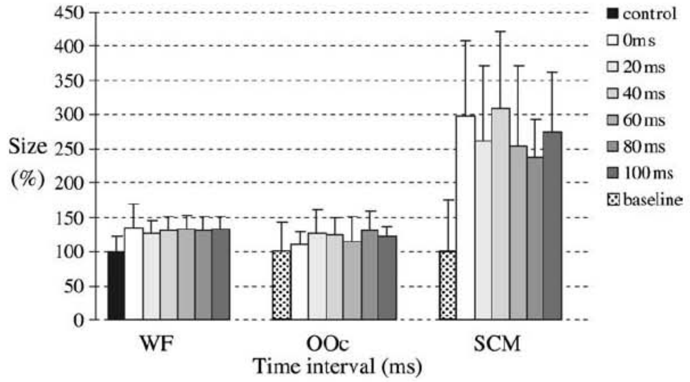


Fig. 2 Columns representing the mean size, and one standard deviation, of the EMG activity of the wrist flexors (*WF*), the orbicularis oculi (*OOc*) and the sternocleidomastoid muscles (*SCM*). Data on the wrist flexors are represented in percentage of the EMG activity in control trials (first column on the left). Data on the orbicularis oculi and the sternocleidomastoid muscles are represented in percentage of baseline trials (first column on the left for each muscle). The remaining columns represent the data from trials in which the startling auditory stimulus was delivered at intervals 0, 20, 40, 60, 80, and 100 ms after the imperative signal

Startle reaction

The blink response, as evidenced by EMG activity in the OOc, has been used extensively as an early indicator of a startle because of its short latency and reliability (Graham 1975; Davis et al. 1982; Wilkins et al. 1986; Blumenthal et al. 2005). After the OOc, activity in the SCM muscle is the next most frequent and most reliable measure of the startle response.

In our experiment, both the OOc and the SCM showed a larger size of the response to the SAS in tests than in baseline trials. However, differences between baseline and test trials were statistically significant only in the SCM. This may be the consequence of a larger degree of habituation in the SCM than in the OOc in baseline trials. This is consistent with previously published observations in the habituation of the startle reaction (Brown et al. 1991; Valls-Solé et al. 1997). In contrast with the marked habituation of the responses to SAS in baseline trials, those obtained in test trials showed substantially less habituation, giving rise to a larger mean value in test trials than in baseline trials.

The response to the acoustic startle (SAS) is determined by stimulus parameters such as its intensity, rise time and duration (Blaszczyk 2003). These parameters were unchanged in baseline and test trials in our experiment. Therefore, the increment of SizeOOc and SizeSCM in test trials suggests that the excitability of the reticulospinal tract (activated by the SAS) increases in a condition of preparation with respect to rest. In agreement with that, we found an increase in the EMG activity of the SCM when a SAS was presented together with the IS in comparison to when it was presented alone, an observation reported also before by Siegmund et al. (2001) and Carlsen et al. (2003). However, no further increase of response size was observed when SAS was presented at time intervals approaching the EMG onset. The size of the startle response is likely to be the result of the number of giant neurons recruited in the nucleus reticularis pontis caudalis in response to SAS (Yeomans and Frankland 1995). Therefore, the absence of changes in the size of the startle response in preparation for execution of a ballistic movement is consistent with the absence of changes in the level of excitability of the brainstem neurons responsible for the generation of the startle reaction. Our results suggest that the necessary increase of excitability required for movement execution does not involve the subcortical motor structures activated by a SAS.

Reaction time

As expected, in test trials, reaction time was significantly shorter than in control trials. This observation has been previously reported and may be defined as the StartReact phenomenon (Valls-Solé et al. 1999; Siegmund et al. 2001; Carlsen et al. 2003, 2004a, b). The startle-induced release of activity at a subcortical level can be responsible for the StartReact effect. The acceleration takes place with no changes in the characteristics of the three bursts EMG pattern. This could be explained by the fact that the motor program prepared for execution in a simple reaction time task experiment is already built in the structures activated by the startling stimulus at the time of arrival of the loud auditory input. Preliminary observations indicate that the program for execution of a ballistic movement is already represented in subcortical structures some time before the presentation of the IS, since the same three burst pattern can be triggered if the SAS is applied a few 100 ms before the IS (Valls-Solé 2004). In the study reported here, the three burst pattern is activated at a latency compatible with the startle reaction from the SAS at progressively longer time intervals from the IS. However, even though the size of the first agonist burst of the flexor muscle is larger in test trials than in control trials, it does not increase further along the intervals examined. This is consistent with the SAS triggering the same unmodified motor program at the various intervals tested after the IS.

The exact contribution of the subcortical motor pathways to the execution of a ballistic movement is not completely known. Our results suggest that their excitability is already increased at the time of the IS and it does not increase further when approaching the onset of EMG activity. Therefore, we may speculate on the existence of a mechanism that maintains the subcortical motor pathways ready to be triggered, just under the level required for executing the intended movement. The giant neurons of the reticularis pontis caudalis are known to send excitatory projections to the limb motoneurons (Yeomans and Frankland 1995). We may assume that, after reaching a certain level of excitability, the motor commands will be issued and the muscles inevitably activated. For adequately performing a ballistic movement, the level of excitability of subcortical structures must be high enough for the movement to be executed at the arrival of the appropriate command and low enough for it not to be released prematurely. This suggests the existence of both excitatory and inhibitory actions.

Subjects performing a simple reaction time task are fully aware of the movement characteristics and may prepare the structures of the execution channel well in advance of the presentation of the imperative signal (Valls-Solé 2004). We think that such preparation implies the subcortical level, and the pathways activated by the SAS are an important part of it. In our experiment, the SAS provided the required input for the system to execute the whole motor program before issuing a voluntary command. In a non-experimental situation, the highly excitable subcortical motor tracts would require only an excitatory input from the descending tracts for their activation. When performing a ballistic movement voluntarily, such ultimate step in the increase of motor pathways excitability generates at a cortical level and is transmitted downwards via cortico-subcortical tracts. The increase in corticospinal tract excitability, which is responsible for the increase in the size of the MEP taking place 60–100 ms before the onset of EMG activity (Pascual-Leone et al. 1992; Davey et al. 1998), would serve as the trigger for the intended movement, conveniently prepared and ready for execution at subcortical level.

References

Blaszczyk JW (2003) Startle response to short acoustic stimuli in rats. Acta Neurobiol Exp 63:25–30

Blumenthal TD, Cuthbert BN, Filion DL, Hackley S, Lipp OV, van Boxtel A (2005) Committee report: guidelines for human startle eyeblink electromyographic studies. Psychophysiology 42:1–15

Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD (1991) New observations on the normal auditory startle reflex in man. Brain 114:1891–1902

Carlsen AN, Hunt MA, Inglis JT, Sanderson DJ, Chua R (2003) Altered triggering of a prepared movement by a startling stimulus. J Neurophysiol 89:1857–1863

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004a) Prepared movements are elicited early by startle. J Mot Behav 36:253–264

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004b) Can prepared responses be stored subcortically? Exp Brain Res 159:301–309

Castellote JM, Valls-Solé J, Sanegre MT (2004) Ballistic reactions under different motor sets. Exp Brain Res 158:35–42

Davey NJ, Rawlinson SR, Maskill DW, Ellaway PH (1998) Facilitation of a hand muscle response to stimulation of the motor cortex preceding a simple reaction task. Motor Control 2:241–250

Davis M, Gendelman DS, Tischler MD, Gendelman PM (1982) A primary acoustic startle circuit: lesion and stimulation studies. J Neurosci 2:791–805

Graham FK (1975) The more or less startling effects of weak prestimulation. Psychophysiology 12:238–248

Evarts EV (1974) Precentral and postcentral cortical activity in association with visually triggered movement. J Neurophysiol 37:373–381

Hallett M, Shahani BT, Young RR (1975) EMG analysis of stereotyped voluntary movements in man. J Neurol Neurosurg Psychiatry 38:1154–1162

Jahanshahi M (2003) Reaction time as an index of motor preparation/programming and speed of response initiation. In: Hallett M (ed) Movement disorders handbook of clinical neurophysiology, vol 1. Elsevier, Amsterdam, pp 203–229

Pascual-Leone A, Valls-Solé J, Wassermann EM, Brasil-Neto J, Cohen LG, Hallett M (1992) Effects of focal transcranial magnetic stimulation on simple reaction time to acoustic, visual and somatosensory stimuli. Brain 115:1045–1059

Siegmund GP, Inglis JT, Sanderson DJ (2001) Startle response of human neck muscles sculpted by readiness to perform ballistic head movements. J Physiol 535:289–300

Starr A, Caramia M, Zarola F, Rossini PM (1988) Enhancement of motor cortical excitability in humans by non-invasive electrical stimulation appears prior to voluntary movement. Electroencephalogr Clin Neurophysiol 70:26–32

Valls-Solé J, Solé A, Valldeoriola F, Muñoz E, González LE, Tolosa ES (1995) Reaction time and acoustic startle in normal human subjects. Neurosci Lett 195:97–100

Valls-Sole J, Valldeoriola F, Tolosa E, Nobbe F (1997) Habituation of the auditory startle reaction is reduced during preparation for execution of a motor task in normal human subjects. Brain Res 751:155–159

Valls-Solé J, Rothwell JC, Goulart F, Cossu G, Muñoz E (1999) Patterned ballistic movements triggered by a startle in healthy humans. J Physiol 516:931–938

Valls-Solé J (2004) Contribution of subcortical motor pathways to the execution of ballistic movements. In: Hallett M, Phillips LH, Schomer DL, Massey JM (eds) Advances in clinical neurophysiology, vol 57. Elsevier, Amsterdam, pp 554–562

Wilkins DE, Hallett M, Wess MM (1986) Audiogenic startle reflex of man and its relationship to startle syndromes. Rev Brain 109:561–573

Yeomans JS, Frankland PW (1995) The acoustic startle reflex: neurons and connections. Brain Res Brain Res Rev 21:301–314

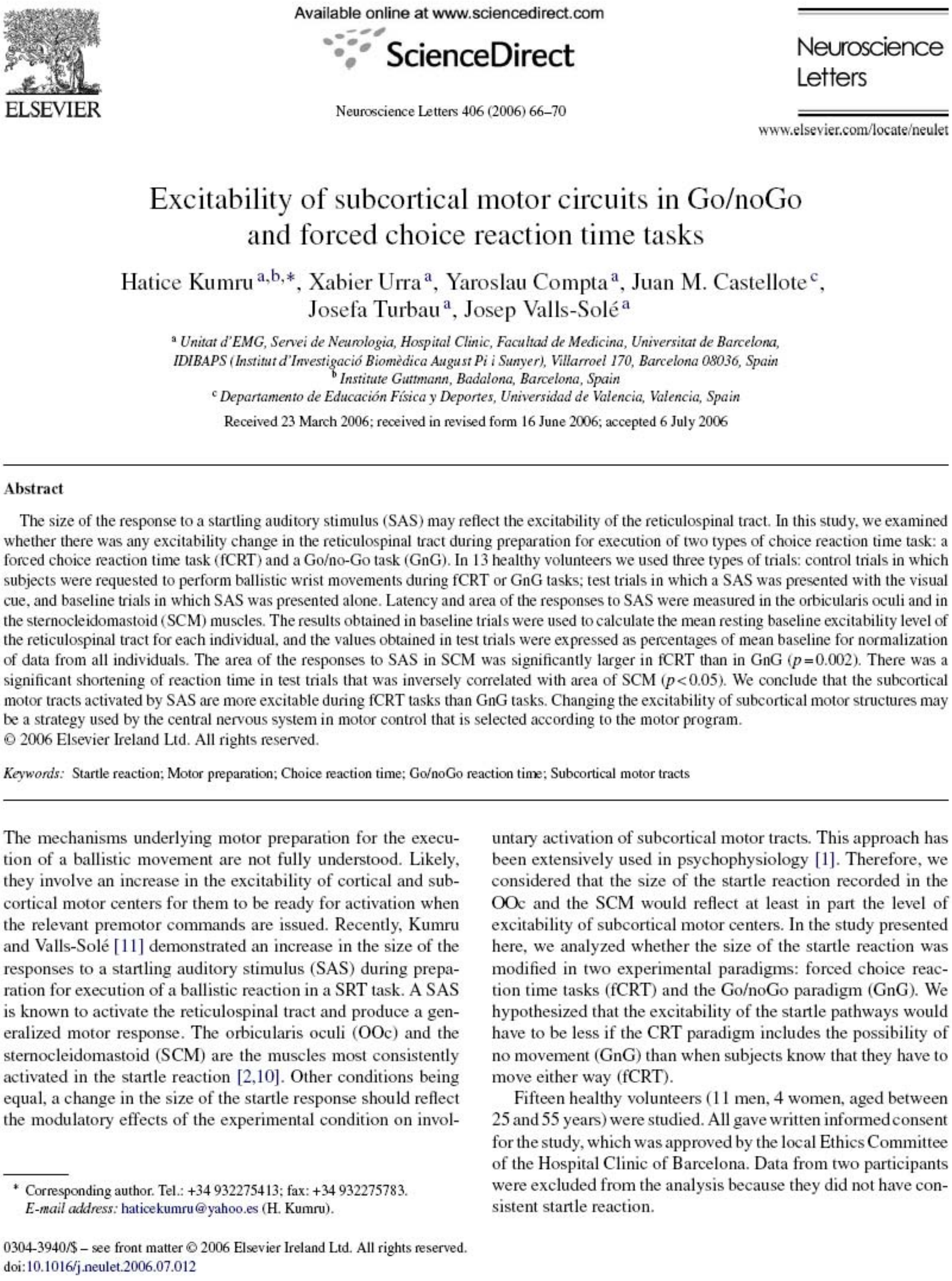
II. PUBLICACIÓN

Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks.

Neuroscience Letters. 2006;406:66-70.

7.2. La preparación subcortical motora ocurre no solamente en el tiempo de reacción simple sino que también se observa en tareas de tiempo de reacción de elección. Por ejemplo, en aquellas ocasiones en las que los sujetos se enfrentan con un número limitado de posibilidades e incluso en casos en que existe la posibilidad de no reacción.

En el estudio de la excitabilidad de los circuitos motores subcorticales en casos de Go/noGo y tREF, los sujetos voluntarios sanos muestran un cierto grado de preparación antes de la presentación de la señal imperativa y, de esta manera, el estímulo de sobresalto facilita la ejecución del programa motor que ya está preparado.



ELSEVIER
Available online at www.sciencedirect.com
ScienceDirect
Neuroscience Letters 406 (2006) 66–70
Neuroscience Letters
www.elsevier.com/locate/neulet

Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks

Hatice Kumru[a,b,*], Xabier Urra[a], Yaroslau Compta[a], Juan M. Castellote[c], Josefa Turbau[a], Josep Valls-Solé[a]

[a] *Unitat d'EMG, Servei de Neurologia, Hospital Clinic, Facultad de Medicina, Universitat de Barcelona, IDIBAPS (Institut d'Investigació Biomèdica August Pi i Sunyer), Villarroel 170, Barcelona 08036, Spain*
[b] *Institute Guttmann, Badalona, Barcelona, Spain*
[c] *Departamento de Educación Física y Deportes, Universidad de Valencia, Valencia, Spain*

Received 23 March 2006; received in revised form 16 June 2006; accepted 6 July 2006

Abstract

The size of the response to a startling auditory stimulus (SAS) may reflect the excitability of the reticulospinal tract. In this study, we examined whether there was any excitability change in the reticulospinal tract during preparation for execution of two types of choice reaction time task: a forced choice reaction time task (fCRT) and a Go/no-Go task (GnG). In 13 healthy volunteers we used three types of trials: control trials in which subjects were requested to perform ballistic wrist movements during fCRT or GnG tasks; test trials in which a SAS was presented with the visual cue, and baseline trials in which SAS was presented alone. Latency and area of the responses to SAS were measured in the orbicularis oculi and in the sternocleidomastoid (SCM) muscles. The results obtained in baseline trials were used to calculate the mean resting baseline excitability level of the reticulospinal tract for each individual, and the values obtained in test trials were expressed as percentages of mean baseline for normalization of data from all individuals. The area of the responses to SAS in SCM was significantly larger in fCRT than in GnG ($p = 0.002$). There was a significant shortening of reaction time in test trials that was inversely correlated with area of SCM ($p < 0.05$). We conclude that the subcortical motor tracts activated by SAS are more excitable during fCRT tasks than GnG tasks. Changing the excitability of subcortical motor structures may be a strategy used by the central nervous system in motor control that is selected according to the motor program.

Keywords: Startle reaction; Motor preparation; Choice reaction time; Go/noGo reaction time; Subcortical motor tracts

---

The mechanisms underlying motor preparation for the execution of a ballistic movement are not fully understood. Likely, they involve an increase in the excitability of cortical and subcortical motor centers for them to be ready for activation when the relevant premotor commands are issued. Recently, Kumru and Valls-Solé [11] demonstrated an increase in the size of the responses to a startling auditory stimulus (SAS) during preparation for execution of a ballistic reaction in a SRT task. A SAS is known to activate the reticulospinal tract and produce a generalized motor response. The orbicularis oculi (OOc) and the sternocleidomastoid (SCM) are the muscles most consistently activated in the startle reaction [2,10]. Other conditions being equal, a change in the size of the startle response should reflect the modulatory effects of the experimental condition on involuntary activation of subcortical motor tracts. This approach has been extensively used in psychophysiology [1]. Therefore, we considered that the size of the startle reaction recorded in the OOc and the SCM would reflect at least in part the level of excitability of subcortical motor centers. In the study presented here, we analyzed whether the size of the startle reaction was modified in two experimental paradigms: forced choice reaction time tasks (fCRT) and the Go/noGo paradigm (GnG). We hypothesized that the excitability of the startle pathways would have to be less if the CRT paradigm includes the possibility of no movement (GnG) than when subjects know that they have to move either way (fCRT).

Fifteen healthy volunteers (11 men, 4 women, aged between 25 and 55 years) were studied. All gave written informed consent for the study, which was approved by the local Ethics Committee of the Hospital Clinic of Barcelona. Data from two participants were excluded from the analysis because they did not have consistent startle reaction.

---

[*] Corresponding author. Tel.: +34 932275413; fax: +34 932275783.
E-mail address: haticekumru@yahoo.es (H. Kumru).

0304-3940/$ – see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.neulet.2006.07.012

Subjects were sitting on a chair with padded armrests, facing a 14-in. computer monitor, situated at approximately 50 cm before the subjects' eyes. Their forearms and hands were firmly attached to a device made of two joined metallic platforms, in such a way that the wrist had only 1° of freedom for flexion-extension movements in the horizontal plane. A potentiometer, built in the hinge joining forearm and hand platforms, was used to record wrist displacement. Silver–silver chloride surface electrodes were used to record the electromyographic activity (EMG) of the right OOc and SCM, and of the wrist flexor (WF) muscles of both sides. The EMG activity was amplified using a conventional EMG machine (Mystro5Plus electromyograph; Oxford Instruments, Surrey, UK) with band pass frequency filters between 50 and 1000 Hz. All EMG and movement signal recordings were printed on thermosensitive paper for off-line analysis.

Subjects were requested to react to a visual cue appearing in the computer's monitor. A 1 × 1 cm white cross was presented in the center of an otherwise black screen, serving as the forewarning for the imperative signal (IS) and as a gaze fixation point. The IS was a 5 × 5 cm square that appeared after a fixed foreperiod of 2000 ms on the right or left sides of the screen, at a distance of 5 cm from the fixation point. One second after the appearance of the small cross on the computer screen a pulse was generated by the computer to trigger the electromyograph.

In some trials at random (see below), presentation of the IS was accompanied by a loud auditory stimulus, capable of producing a startle reaction. This was obtained by discharging the coil from a magnetic stimulator over a metallic platform, which produces a sound of an intensity of 130 dB sound pressure level (SPL), measured at a distance of 1 m from the source with a Brüel and Kjaer Impulse Precision Sound Level Meter type 2204 [16].

Subjects received full verbal instructions on the general experimental procedure, which involved two separate sessions, with a short break in between:

1. Forced choice reaction time task (fCRT): In this session, subjects were requested to perform a rapid wrist flexion with their right hand as quickly as possible when the IS appeared on the right side of the screen and with their left hand when the IS appeared on the left side of the screen.
2. Go/noGo task: This experiment was subdivided into two parts—GnG right and GnG left. In GnG right, subjects had the instruction to perform a rapid wrist flexion with their right hand if the IS appeared on the right side and not to react if the IS appeared on the left side. In GnG left, the subjects had to react with their left hand if the IS appeared on the left side and they had the instruction not to react when the IS appeared on the right side.

In each session, the experiments were conducted using three different types of trials: control trials were those in which there was only the presentation of the IS. Baseline trials were those in which only the SAS was presented with no previous instruction. Test trials were those in which a SAS was presented together with the IS. The side of IS was pseudorandomized within and between trials. The order of the sessions was interchanged randomly among subjects. We obtained 45 trials for fCRT, GnG right and GnG left: thirty control trials, 10 test trials and 5 baseline trials. Test and baseline trials were intermingled randomly among control trials.

In control and test trials, we measured reaction time as the onset latency of EMG activity recorded in the WF (LatWF) from the IS. In test and baseline trials, we determined response onset latency (LatOOc, LatSCM) at the point where the EMG activity increased above 50 μVs from mean baseline for at least 20 ms. We measured the area of the EMG activity in a time window after IS, ranging from 20 to 150 ms for the OOc and 20 to 180 for the SCM. In graphs printed in thermosensitive paper, we scanned the graphs and used the AutoCAD 2006 (Autodesk, California) to measure the area using polyline within the fixed time period (AreaOOc and AreaSCM, respectively).

We also calculated the number of correct responses, expressed as the mean number of trials in which the subject performed the correct task, in percentage of the total number of trials, for each session.

The data obtained in GnG right and GnG left trials were collapsed to obtain a single group for each subject. Also, we averaged the data obtained in fCRT for right and left hand. We used the two factors ANOVA (task "fCRT-GnG" and trial type "control-test") to determine whether the presence of SAS had any effect on LatWF, as well as on the percentage of correct response. One-way ANOVA was used to compare LatOOc and LatSCM between baseline, fCRT and GnG. For AreaOOc and AreaSCM, we calculated the individual's percentages with respect to the corresponding mean data in baseline trials. To compare the percentage AreaOOc and AreaSCM between fCRT and GnG, we used Student *t*-test or Wilcoxon *t*-test, depending on whether the data followed a normal or non normal distribution. The level of statistical significance was set at $p < 0.05$. The Spearman rank correlation test was used to calculate the relation between reaction time tasks and startle reaction variables.

The experiments were completed without any difficulty by all subjects. Representative examples of recordings taken from one subject are shown in Fig. 1. Responses to SAS in baseline trials had a mean latency (and one standard deviation) of 35.1 ± 4.8 ms in the OOc, and 69.4 ± 7.7 ms in the SCM. As expected, AreaOOc and AreaSCM were very variable between subjects. In baseline trials, the mean values were 7536 ± 3662 μV ms for the OOc and 4505 ± 8296 μV ms for the SCM. The Table 1 reports the latency and area of the responses recorded in test trials. There were no differences between fCRT, GnG, and baseline for LatOOc ($F(2, 36) = 0.5$; $p = 0.6$) or for LatSCM ($F(2,$

Table 1
Responses recorded in the orbicularis oculi and sternocleidomastoid muscles in test trials

	Latency OOc	Latency SCM	% of AreaOOc	% of AreaSCM
fCRT	34.4 ± 5	66.9 ± 20.8	105 ± 21	125 ± 37
GnG	34 ± 4	70 ± 18	92 ± 19	71 ± 38*

Figures are the mean values and one standard deviation of latency, in ms, and mean area, in %. OOc: orbicularis oculi muscle, SCM: the sternocleidomastoid muscle, GnG: Go/noGo task, fCRT: forced choice reaction time task.

* Statistically significantly different from fCRT.

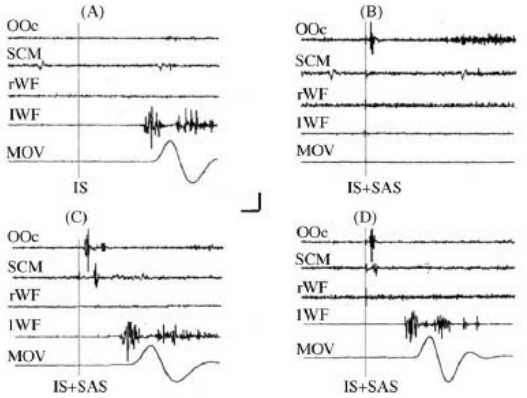


Fig. 1. Selected recordings from a single typical participant reacting with the left hand. (A) Control trial obtained in the experimental condition GnG in response to a Go stimulus. (B) Test trial obtained in the experimental condition GnG in response to a noGo stimulus. (C) Test trial obtained in the experimental condition fCRT in response to a left side stimulus. (D) Test trial obtained in the experimental condition GnG in response to a Go stimulus. The gain was 0.1 mV for OOc and SCM, 0.5 mV for WF and 5 mV for Mov. The horizontal bar stands for 100 ms. GnG: Go/noGo task, fCRT: forced choice reaction time task, OOc: orbicularis oculi, SCM: sternocleidomastoid, rWF: right wrist flexors, lWF: left wrist flexors, MOV: signal from the movement transducer, IS: imperative signal, SAS: startling auditory stimulus.

36) = 0.2; $p = 0.8$). The percentage change of AreaSCM was significantly larger in fCRT than in GnG (non-normal distribution; Wilcoxon test; $p = 0.0021$). The percentage change in AreaOOc was also larger in fCRT than in GnG, but the differences did not reach statistical significance (normal distribution; Student *t*-test; $p = 0.26$). There was significant inverse relation between LatWF and AreaSCM ($r = -0.573$; $p = 0.051$ for GnG; for fCRT; $r = -0.68$; $p = 0.022$). No other relation was found between the other variables.

In control trials, mean LatWF was 324 ms ± 55 ms for fCRT and 343 ms ± 77 ms for GnG. These values shortened in test trials to a mean of 257 ms ± 62 ms for fCRT and 297 ms ± 60 ms for GnG. Fig. 2 shows the mean latency recorded in WF. A two-factor ANOVA showed a significant effect of trial type on LatWF, with a significantly shorter LatWF in test than in control trials ($F = 10.3$; $p = 0.002$). However, there was no significant effect of task ($F = 2.7$; $p = 0.1$), and no interaction between trial type and task ($F = 0.3$; $p = 0.6$).

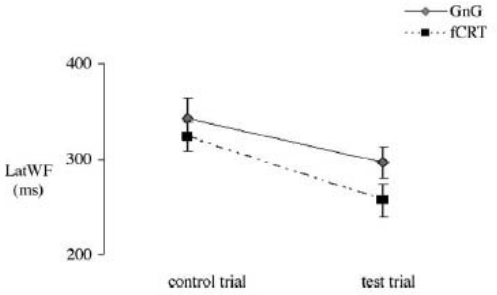


Fig. 2. Mean latencies of the EMG activity (±standard error) recorded in wrist flexor muscles (LatWF) in control trials and test trials, reported in ms for Go/noGo (GnG), and forced choice reaction time (fCRT).

The mean percentage of correct responses was 95.5% ± 6.2% in control and 86.9% ± 9.1% in test trials for GnG, and 99.2% ± 2.8% in control and 91.3% ± 8.5% in test trials for fCRT. A two-factor ANOVA showed a significant effect of experimental session, with lower percentage of correct responses in GnG than in fCRT ($F = 4.3$; $p = 0.04$), and a significant effect of trial type, with lower percentage of correct responses in test than in control trials ($F = 17.4$; $p < 0.001$). There were no interaction effects ($F = 0.27$; $p = 0.87$).

All errors in control trials and most of them in test trials consisted in movement execution with the dominant right hand in fCRT when IS appeared on the left side. The other errors in test trials in fCRT were either the reaction with both hands or the reaction with left hand when the IS appeared on the right side. All errors in control trials and most of them in test trials in GnG consisted in movement execution when the subject received the noGo instruction. A small number of errors in GnG consisted in the inhibition of reaction when subjects had the Go instruction.

The results reported here lead to two points of discussion: (1) the excitability of the subcortical motor pathways activated by SAS (OOc and SCM) was less marked in the GnG task, which includes a 'not-to-move' condition, than in the fCRT task, which requires performing either one or another movement. (2) The reaction time was significantly shorter in test than in control trials in both CRT tasks used in our study and there was an inverse correlation between reaction time and area of the startle reaction.

AreaSCM and AreaOOc were larger in fCRT than in baseline trials, while they were smaller in GnG than in baseline trials. These results are compatible with a relatively enhanced excitability of the subcortical motor pathways activated by a SAS in CRT tasks requiring performing a movement in all conditions, and relatively depressed excitability when the task includes a 'not-to-move' option, than in resting situation. A substantial difference between the two tasks should refer to the amount of inhibitory activity used to stop any intention to move. The GnG process seems to consist of several sub-processes, namely: discrimination of the stimuli, decision to move/not to move, and excitation/inhibition of the motor action. These sub-processes must be carried out in various brain areas [14].

Inhibition of responding can take place at various levels. The existence of cortical inhibitory mechanisms contributing to the control of motor actions has been previously reported [7]. Studies done with transcranial magnetic stimulation (TMS) and event related potentials (ERP) have shown a decrease of motor cortical excitability in the 'no-go' trials of the GnG condition [14,7,6]. The active inhibition of a movement involves an increase in synaptic activity studied by fMRI in humans [17]. Cortical motor networks integrate facilitatory and inhibitory activity that may be selected depending on the context. It has recently been shown that cortical excitability is reduced for "Stop" trials relative to

"Go" trials from 140 ms after IS and short interval intracortical inhibition is greater for "Stop" trials compared with "Go" trials [4].

It is possible that less excitability of the startle response in GnG in comparison to fCRT is due to activation of some of the circuits with inhibitory influences over the nuclei of the reticular formation. One of the most studied mechanisms of control of the startle reaction is prepulse inhibition [9]. Experimental activation of prepulse inhibition of the startle reaction in the context of a reaction time task paradigm showed that the inhibitory effect of the prepulse over the startle reaction was maintained without affecting the startle-induced acceleration of reaction time [15].

Many factors could contribute to modulation of the area and habituation of the startle reaction in our study, including affective and attentional aspects [12]. Likely, our subjects were choosing the strategy judged most convenient to comply with the task. This could include expectation for a spatial location of the IS in the GnG condition. In theory, if subjects were neglecting visual cues assigned to the noGo condition, the task could transform in a kind of simple reaction time. However, our subjects had to be prepared for a fast reaction. Therefore, even if strategies involving expectation and selective attention were used, there was the need for inhibiting the prepared reaction in the noGo trials. Such inhibitory component of the preparation is consistent with the reduced area of the startle reaction in GnG in comparison to baseline or fCRT. The degree of attention that the subjects paid to the IS or to the response they were instructed to do is another factor that has to be taken into account in search for an explanation of differences in the level of excitability of subcortical motor structures between GnG and fCRT. Preparation for execution of a movement is likely more prominent if subjects engage in a 'motor set', i.e., they concentrate in the response to be performed than if they engage in a 'sensory set', i.e., they concentrate on detection of the imperative cue [5]. In our experiments, subjects were always instructed to be ready to move, and we stressed the point that they had to perform their reaction as fast as possible. However, engaging in a 'response set' might have been more difficult to do in the GnG condition if subjects wanted to avoid errors of commission.

In our subjects, LatWF was significantly shorter in test trials than in control trials. However, the percentage shortening with respect to control trials was clearly less than the one occurring in SRT [16,3]. It is believed that subcortical motor preparation can not take place in the case of CRT because the response to be performed is not fully known prior to the presentation of the IS [8]. The logical consequence of acceleration of movement execution in CRT tasks is increased number of erroneous movements. Therefore, the prediction would be that reduced preparation would lead to fewer errors.

In our study, reaction time was shortened with SAS in CRT paradigms, an observation that has not been reported in other experiments of a similar type [3]. Indeed, intersensory facilitation could partially account for reaction time shortening [13]. The SAS resulted in acceleration of RT in our study in CRT paradigms. In particular, the startle response may act to increase the neural excitability and decrease neural threshold throughout the motor system, resulting in movement production with shorter premotor RT, which one previously observed through the use of transcranial magnetic stimulation in SRT and GnG [13]. We have found that there was a significant inverse relation between increase in AreaSCM and shortening in LatWF. It is unlikely that intersensory facilitation could lead to changes in the area of the startle reaction. Therefore, we think that the reaction time shortening in relation to the presentation of a SAS together with the IS may be due to the overlap between two effects: the increase in the energy of the sensory cue and the intersensory facilitation that this may produce, and a specific effect of the activation of subcortical structures. It is possible that both effects were present and influencing the results of our study.

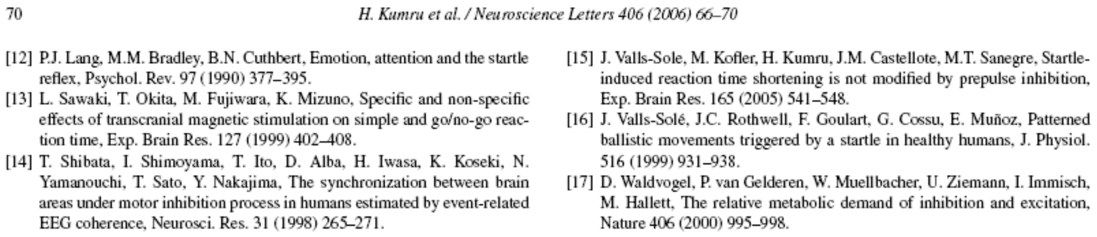
We conclude that, when subjects have motor preparation before IS, a startling stimulus facilitates releasing of the motor program that has been prepared even in paradigms of CRT. In some occasions, this situation may lead to the execution of actions that the subject would not have actually wanted to do. Even though the preparation implies an increasing probability of errors in choice responding, it is conceivable that, in conditions requiring movements at a high speed, subjects prefer to prepare their motor system for a reaction, rather than be at rest, before knowing exactly what movement would be required.

Acknowledgment

Part of this work was accomplished thanks to grant P1040970 from Instituto de Salud Carlos III.

References

[1] M.M. Bradley, B. Moulder, P.J. Lang, When good things go bad: the reflex physiology of defense, Psychol. Sci. 16 (2005) 468–473.
[2] P. Brown, J.C. Rothwell, P.D. Thompson, T.C. Britton, B.L. Day, C.D. Marsden, New observations on the normal auditory startle reflex in man, Brain 114 (1991) 1891–1902.
[3] A.N. Carlsen, R. Chua, J.T. Inglis, D.J. Sanderson, I.M. Franks, Can prepared responses be stored subcortically? Exp. Brain Res. 159 (2004) 301–309.
[4] J.P. Coxon, C.M. Stinear, W.D. Byblow, Intracortical inhibition during volitional inhibition of prepared action, J. Neurophysiol. 95 (2006) 3371–3383.
[5] L. Henderson, W.H. Dittrich, Preparing to react in the absence of uncertainty: I. New perspectives on simple reaction time, Br. J. Physiol. 89 (1998) 531–554.
[6] M. Hoshiyama, S. Koyama, Y. Kitamura, M. Shimojo, S. Watanabe, R. Kakigi, Effects of judgement process on motor evoked potentials in Go/No-go hand movement task, Neurosci. Res. 24 (1996) 427–430.
[7] S.R. Jackson, G.M. Jackson, M. Roberts, The selection and suppresion of action: ERP correlates of executive control in humans, Neuroreport 10 (1999) 861–865.
[8] S.T. Klapp, Reaction time analysis of two types of motor preparation for speech articulation: action as a consequence of chunks, J. Mot. Behav. 35 (2003) 135–150.
[9] M. Koch, Schnitzler HU The acoustic startle response in rats. Circuits mediating evocation, inhibition and potentiation, Behav. Brain Res. 89 (1997) 35–49.
[10] M. Kofler, J. Muller, L. Reggiani, J. Valls-Sole, Influence of age on auditory startle responses in humans, Neurosci. Lett. 307 (2001) 65–68.
[11] H. Kumru, J. Valls-Solé, Excitability of the pathways mediating the startle reaction before execution of a voluntary movement, Exp. Brain Res. 169 (2006) 427–432.



[12] P.J. Lang, M.M. Bradley, B.N. Cuthbert, Emotion, attention and the startle reflex, Psychol. Rev. 97 (1990) 377–395.

[13] L. Sawaki, T. Okita, M. Fujiwara, K. Mizuno, Specific and non-specific effects of transcranial magnetic stimulation on simple and go/no-go reaction time, Exp. Brain Res. 127 (1999) 402–408.

[14] T. Shibata, I. Shimoyama, T. Ito, D. Alba, H. Iwasa, K. Koseki, N. Yamanouchi, T. Sato, Y. Nakajima, The synchronization between brain areas under motor inhibition process in humans estimated by event-related EEG coherence, Neurosci. Res. 31 (1998) 265–271.

[15] J. Valls-Sole, M. Kofler, H. Kumru, J.M. Castellote, M.T. Sanegre, Startle-induced reaction time shortening is not modified by prepulse inhibition, Exp. Brain Res. 165 (2005) 541–548.

[16] J. Valls-Solé, J.C. Rothwell, F. Goulart, G. Cossu, E. Muñoz, Patterned ballistic movements triggered by a startle in healthy humans, J. Physiol. 516 (1999) 931–938.

[17] D. Waldvogel, P. van Gelderen, W. Muellbacher, U. Ziemann, I. Immisch, M. Hallett, The relative metabolic demand of inhibition and excitation, Nature 406 (2000) 995–998.

III. PUBLICACIÓN

The effects of a prepulse on the startreact phenomenon.

Suppl Clin Neurophysiol. 2006; 58: 101-9.

7.3. La reacción de sobresalto y los efectos de un estímulo en el tiempo de reacción son dos efectos diferentes, que responden de manera diferente a la inhibición por prepulso.

Los músculos que no participan directamente en la reacción retienen la reactividad al sobresalto y el efecto de prepulso puede expresarse plenamente al no ser incluido en el aumento de excitabilidad típico del programa motor preparatorio. Más estudios sobre la relación entre las acciones voluntarias y reflejas son necesarios para entender completamente el papel de los circuitos motores subcorticales en la organización y ejecución de los actos motores humanos.

Brainstem Function and Dysfunction (Supplements to Clinical Neurophysiology, Vol. 58)
Editors: G. Cruccu, M. Hallett

Chapter 9

The effects of a prepulse on the StartReact phenomenon

Hatice Kumru[a], Josep Valls-Solé[a,*], Markus Kofler[b],
Juan Castellote[c] and Teresa Sanegre[c]

[a]*Unitat d'EMG, Servei de Neurologia, Universitat de Barcelona, IDIBAPS (Institut d'Investigació Biomèdica August Pi i Sunyer), Barcelona (Spain)*
[b]*Department of Neurology, Hospital HochZirl, A-6170 Zirl (Austria)*
[c]*Facultad de la Actividad Física y del Deporte, Universidad de Valencia, Valencia (Spain)*

1. Introduction

The StartReact phenomenon is the shortening of the reaction time that takes place when a startling auditory stimulus (SAS) is applied together with the imperative signal in a reaction time task experiment (Valldeoriola et al., 1998; Valls-Solé et al., 1999a). This phenomenon can be the consequence of activation of the subcortical motor pathways holding a representation of the motor program prepared for execution. However, it could also simply be the startle reaction added to the motor program (Siegmund et al., 2001).

The startle reaction is known to be inhibited by a prepulse, a weak stimulus that is unable by itself to trigger a response but causes an effect on a subsequent response-eliciting stimulus (Graham, 1975; Blumenthal and Gescheider, 1987). It is not known whether prepulse inhibition (PPI) is still effective during preparation for movement execution. In this study, we wanted to investigate whether the inhibitory effects of the prepulse were different in the condition of motor preparation with respect to that of unexpectancy, and whether the inhibition of the startle reaction by a prepulse was associated with inhibition of the StartReact phenomenon. We reasoned that this procedure could help in ascertaining whether reflex and volitional components are actually combined in the StartReact phenomenon.

2. Methods

2.1. Subjects

We studied 8 healthy volunteers, 6 men and 2 women, aged between 25 and 52 years. All subjects gave their consent for the study after being fully informed about the nature of the experiments. The study protocol was approved by the local Ethical Committee.

Subjects were asked sit to on a comfortable chair, with their hands resting on armrests. The computer screen was placed at a distance of 1 m from the subject's eyes. First of all, a small cross, the forewarning signal, appeared at the center of the screen to let the subjects know that they should be ready to react at the imperative signal (IS) which was a 5 × 5 cm^2 white square. The foreperiod was fixed at 2 s. The subjects were instructed to react as fast as possible by hitting a switch placed within reaching distance of their right hand. One second after the appearance of the small

---

**Correspondence to*: Josep Valls-Solé, Unitat d'EMG, Servei de Neurologia, Hospital Clínic, Villarroel, 170, Barcelona 08036, Spain.
Tel: 34932275413; Fax: 34 932275783;
E-mail: jvalls@clinic.ub.es

cross on the computer screen (i.e. 1 s before the appearance of the imperative signal), a pulse was generated by the computer to trigger the recording system, a conventional electromyograph (Mystro5Plus; Oxford Instruments, Inc., SA, London).

The startle reaction was recorded with surface electrodes over the right orbicularis oculi muscle and, in two of the subjects, also over the sternocleidomastoid muscle. The EMG activity related to the voluntary action was recorded from the wrist extensor muscles. Prepulse stimuli were weak electrical shocks delivered to the 3rd finger of the left hand through a pair of ring electrodes. Stimulus intensity was between 1.5 and 2.5 times the perception threshold, and we made sure that this stimulus did not elicit any reflex response by itself. The prepulse stimulus was always applied 100 ms before the startling stimulus (Valls-Solé et al., 1999b). The startling auditory stimulus was produced by the discharge of the coil of a magnetic stimulator on top of a metallic platform. This method permits to deliver a loud stimulus (130 dB at a distance of 1 m from the source of the noise), capable of inducing consistent startle responses (Valls-Solé et al., 1999a).

2.2. Procedure

The experiment was composed of seven different conditions, with trials of each condition presented in random order. In all instances, subjects were instructed to react to the presentation of the imperative signal and disregard other events. A free interval of 10–15 s was allowed between two consecutive trials, and an oral instruction to draw the attention of the subject and ask for motor preparation was always given just before onset of each trial, regardless of the trial condition. The conditions were:

(1) Prepulse alone (Prep), in which subjects were presented with the prepulse stimulus alone.
(2) Startle alone (Start), in which subjects were presented with the startling auditory stimulus alone.
(3) Prepulse and startle (PrepStart), in which subjects were presented with the prepulse stimulus 100 ms prior to the auditory stimulus.
(4) Reaction alone (React), in which subjects were presented with the imperative signal only.
(5) Reaction plus startle (StartReact), in which subjects were presented with the imperative signal together with the startling auditory stimulus at the same time.
(6) Prepulse and reaction (PrepReact), in which subjects were presented with the prepulse stimulus preceding the imperative signal by an interval of 100 ms, and
(7) Prepulse, startle, and reaction (PrepStartReact), in which the prepulse stimulus was delivered 100 ms before the simultaneous presentation of the imperative signal and the startling auditory stimulus.

We collected 10 trials for each condition, except for the condition React, which was considered as the reference condition for all results of trials involving reaction time tasks. The condition React was actually considered the default condition, which the experimenter used monotonously between other conditions, to try to break down any possible subject's expectancy of a startling stimulus, as well as to maintain a state of readiness for the performance of a ballistic movement. As a result of that, the total number of trials collected in the condition React was considerably larger than in the other conditions.

2.3. Data reduction and analysis

With regard to the startle-related EMG activity, we determined whether the response was present or not in the orbicularis oculi and sternocleidomastoid muscles, in trials containing a startle (Start, PrepStart, StartReact, and PrepStartReact). When background activity was present, which was often the case in the sternocleidomastoid muscle, we set an arbitrary limit, of a minimum amplitude of 50 μV for a minimum duration of 20 ms above background, for a response to be considered. We determined the presence or not of a response, and the percentage of trials of each type in which there was a response. When the response was present, we measured its latency, in ms from the imperative signal, and its peak-to-peak amplitude, in μV.

With regard to reaction time, we measured the onset latency of the EMG activity (WE-EMG) in React, PrepReact, StartReact, and PrepStartReact trials. Individual mean baseline reaction time was determined for each subject from the trials collected in condition React, and was assigned 100%. The effects of prepulse and startle stimuli on WE-EMG were determined for each condition as a percentage of the mean reaction time measured in React trials. Trials which furnished an incomplete set of data because of failure to move at due time or wrong movement performance, were excluded online, and additional trials were added to obtain the projected number of trials in that condition.

Statistical analysis for comparison of data among trial types was carried out using the analysis of variance (ANOVA). We compared the parametric variables related to the startle-related EMG activity of the orbicularis oculi and sternocleidomastoid muscles (latency and amplitude) among trials containing a startling auditory stimulus. With regard to the reaction time variables (WE-EMG), we calculated their relative values as the percentage change of reaction time in React trials. If necessary, post-hoc comparisons between specific trial types were made using Bonferroni's test. Statistical significance was set at $p < 0.05$.

3. Results

Subjects made spontaneous comments in trials containing either the prepulse or the startling auditory stimulus. In reaction time trials containing the prepulse or the startling auditory stimulus, a few subjects reported spontaneously that some external force made them react and they were somehow surprised to see that they had already done the movement. In some PrepStart, PrepReact, or PrepStartReact trials, a few subjects responded when questioned not to have felt any electrical stimulus at all.

3.1. The effects of the prepulse and the startle on the responses of the orbicularis oculi muscle: Prep, Start, and PrepStart trials

In the condition Prep, no evident responses were observed in any subject. In the condition Start, all subjects had a response in the orbicularis oculi that, in spite of some habituation was present even in the last Start trials of the experiment. Table 1 shows the mean values of reflex response latencies and amplitudes of the orbicularis oculi and of the sternocleidomastoid (in two subjects) for all trials containing a startling auditory stimulus. The EMG activity of the orbicularis oculi was absent or markedly reduced in the PrepStart condition in comparison to Start trials, with a recognizable burst of EMG activity being present in less than 20% of PrepStart trials. Statistical comparison between conditions showed significant differences in the size of the startle response (ANOVA; $F[3,28]=140$;

TABLE 1

MEAN AND SD VALUES ON THE EMG ACTIVITY RELATED TO THE STARTLE REACTION

Trial type	OOc latency (ms)	OOc amplitude (μV)	SCM latency (ms)[d]	SCM amplitude (μV)[d]
Start	48.8 (5.9)	403 (103)	65.1 (6.2)	255.3 (71.1)
PrepStart	43.8 (4.1)	15 (21)[a]	59.8 (7.4)	12.5 (17.7)
StartReact	42.7 (5.0)	603 (89)[b]	63.6 (9.8)	260.0 (113.1)
PrepStartReact[c]	43.8 (4.6)	19 (18)[a]	60.7 (5.9)	18.7 (22.8)

OOc – Orbicularis oculi muscle.
SCM – Sternocleidomastoid muscle.
[a] Significantly smaller ($p<0.001$) with respect to the mean in React trials.
[b] Significantly larger ($p<0.001$) with respect to the mean in React trials.
[c] Calculated only in those trials in which the subjects reacted to the imperative signal (68.8% of the trials).
[d] No statistical analysis done. Data are from two subjects only.

$p<0.0001$). Post-hoc analysis showed that startle responses were significantly larger in the StartReact condition with respect to Start ($p<0.0001$), PrepStart ($p<0.0001$), and PrepStartReact ($p<0.0001$). Furthermore, startle responses were significantly smaller in PrepStart versus Start ($p<0.0001$) and StartReact ($p<0.0001$), and in PrepStartReact versus Start ($p<0.0001$) and StartReact ($p<0.0001$). No differences were found between PrepReact and PrepStartReact conditions ($p=0.7$). No specific statistical analysis was done in the data from the sternocleidomastoid, which had a similar behavior as the data collected in the orbicularis oculi.

No statistically significant differences were observed between conditions with regard to the latency of OOc (ANOVA; $F[3,28]=2.5$; $p=0.08$). Similarly, the data from the sternocleidomastoid obtained in the two patients examined showed no relevant differences regarding onset latency.

3.2. The effects of a startle and prepulse on reaction time: React, PrepReact, StartReact, and PreStartReact trials

Mean values and one standard deviation of the reaction times in React, PrepReact, StartReact, and PrepStartReact conditions are shown in Table 2. As expected, reaction time was significantly shorter in the StartReact than in the React condition (Fig. 1). Reaction time values ranged from 182 to 295 in React trials, and from 68 ms to 168 ms in StartReact trials.

A different situation was observed in PrepReact and PrepStartReact conditions, in which the EMG activity occasionally coincided with or even preceded the presentation of the imperative signal (Fig. 2). When we plotted the number of responses as a function of reaction time, expressed in bins of 25 ms, the histogram had a rather biphasic distribution (Fig. 3). We considered the possibility that, in trials in which there was an early response, subjects reacted to the presentation of the prepulse rather than to the imperative stimulus. Because the StartReact effect has never been reported to have a latency shorter than 65 ms, we chose this cut-off time to differentiate reactions to the imperative signal from those to the prepulse. The latter occurred in 35.0% of the trials in the PrepReact condition, and in 31.2% of the trials in the PrepStartReact condition. These trials were rejected from the statistical analysis.

Statistical analysis of the mean values of WE-EMG onset latencies, calculated only in those trials in which the subjects reacted to the imperative signal, showed significant differences among the four conditions (ANOVA; $F[3,28]=18.8$ $p<0.001$). Post-hoc analysis showed that reaction time was significantly shorter in StartReact trials with respect to React ($p<0.0001$); or PrepReact ($p<0.0001$). However, no differences were observed when comparing StartReact with PrepStartReact ($p=0.8$) or React vs PrepReact ($p=0.9$).

Shortening of reaction time was not significantly different in PrepStartReact trials and in StartReact trials. The differences between the two conditions were found in the size of the startle burst of the orbicularis oculi in all subjects and of the sternocleidomastoid in the two subjects examined. While these responses were larger than the reference values in the StartReact condition, they were markedly reduced in the PrepStartReact condition, to an amount comparable to that seen in the PrepStart condition (Fig. 4).

TABLE 2

MEAN AND SD VALUES ON THE EMG ACTIVITY RELATED TO THE STARTLE REACTION

Trial type	WE-EMG (ms)	WE-EMG (% of react)
React	232.4 (37.1)	100.0 (17.2)
StartReact	144.9 (40.5)[a]	56.9 (11.6)
PrepReact[b]	225.9 (46.6)	96.7 (29.6)
PrepStartReact[b]	121.9 (42.1)[a]	56.6 (10.3)

[a] $p<0.001$ with respect to the mean in React trials.

[b] Calculated only in those trials in which the subjects reacted to the "go" signal (65% of the trials in the PrepReact condition, and 68.8% of the trials in the PrepStartReact condition).

4. Discussion

Probably the most important conclusion of our study is that although a prepulse stimulus had an inhibitory

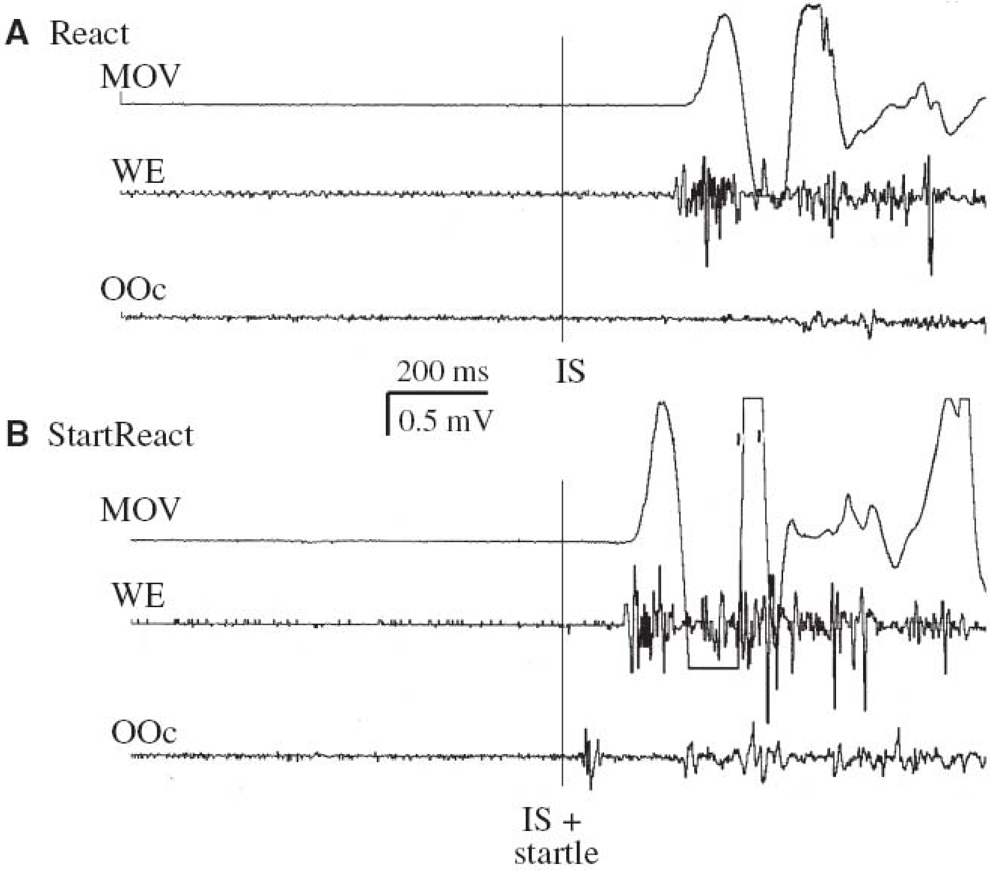


Fig. 1. Examples of a reaction time response in React (A) and StartReact (B) conditions. In this and the subsequent figures, the upper trace represents the hand movement, the middle trace the agonist muscle EMG activity, and the lower trace the orbicularis oculi EMG activity.

effect on the startle reaction even during preparation for a motor task, the effect was limited to the startle reaction itself, and did not influence the startle-induced reaction time acceleration, or StartReact phenomenon. This is consistent with the idea that the startle reaction and the StartReact phenomenon are two different effects of a SAS, with probably different physiological mechanisms.

The StartReact phenomenon may be due to the execution of the voluntary commands through the pathways used for the startle reaction (Valls-Solé et al., 1999a). In this hypothesis, the motor program for a ballistic movement, stored in the central nervous system, is integrated in the startle and forced to be executed throughout, beyond the subject's will. An alternative possibility is that the StartReact phenomenon is the result of a startle reaction being shaped by the presence of the voluntary commands (Siegmund et al., 2001).

Frequently, in our subjects, the prepulse stimulus changed its characteristic physiological properties to

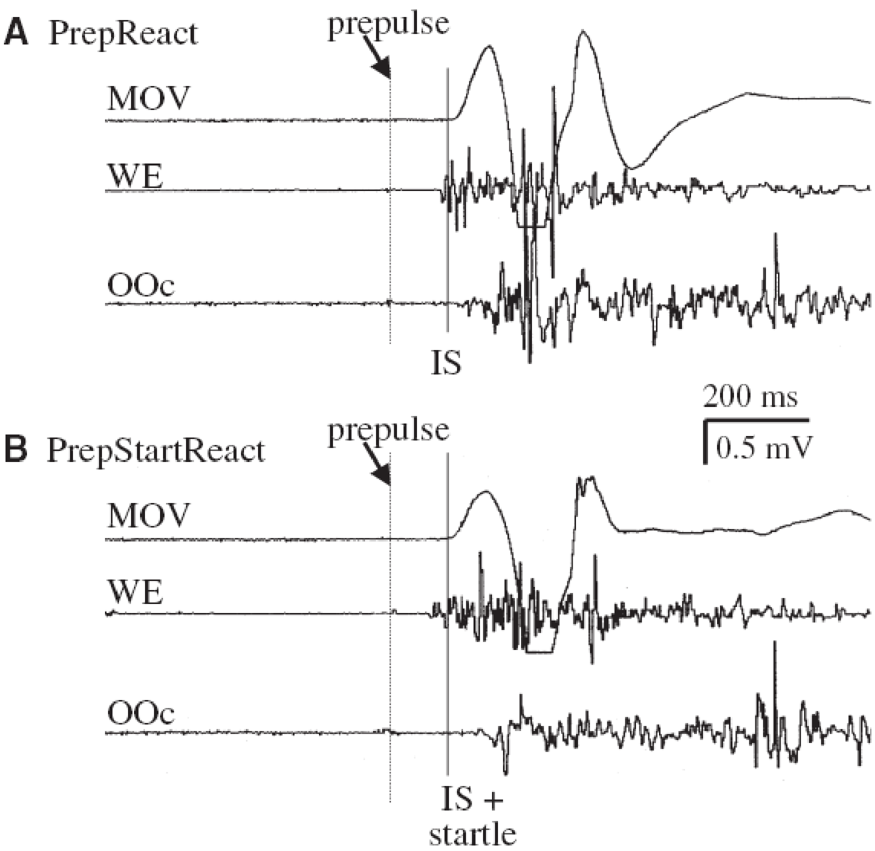


Fig. 2. Examples of a reaction time response in PrepReact (A) and PrepStartReact (B) conditions. Note the early onset of the reaction, with the onset of agonist muscle EMG activity preceding the IS. In these conditions, we considered that the subject reacted to the prepulse stimulus.

take a role similar to that of the startling stimulus itself. In these instances, the prepulse stimulus was able to trigger the entire response, as it is the case with the StartReact phenomenon. To note is that this occurred 100 ms before the actual imperative signal, which leads to the idea that some subjects had reached a sufficient amount of motor preparation by that time for a nearly imperceptible prepulse stimulus to trigger the entire response. In a simple reaction time task paradigm, motor programs should be ready for execution as soon as the imperative signal is detected. In conditions of extreme preparedness, the time involved in processing and decoding the sensory signal may be reduced to zero but, even in these instances, performing a voluntary open-loop ballistic movement will require time for perception and for execution (Henderson and Dittrich, 1998). Full preparedness implies an enhanced excitability of the motor system. Such an increase in excitability has been demonstrated by an increased amplitude of the motor evoked potential in the agonist muscle following transcranial stimulation (Starr et al., 1988; Pascual-Leone et al., 1992), and of the agonist muscle H reflex (Michie et al.,1976; Schieppati et al., 1986), already before the onset of any EMG activity in

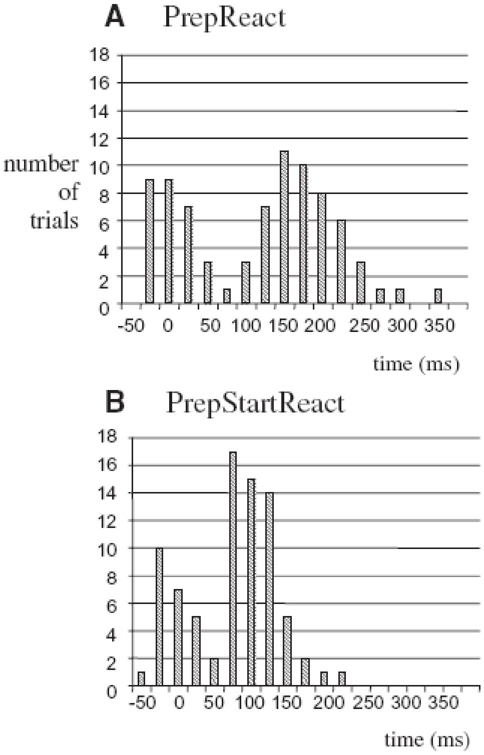


Fig. 3. Histographic representation of the number of trials, distributed according to the time interval of onset of agonist muscle EMG activity (in bins of 25 ms). Note the bimodal distribution, with about 30% of the responses occurring between –50 and +50 ms, thus likely having been triggered by the prepulse.

the target muscle. Previous experiments have shown that such enhanced excitability of the motor system involves also the reticulo-spinal system, with the startle reaction being larger and of reduced habituation in conditions of motor preparation (Valls-Solé et al., 1995, 1997). One possible consequence of such a state of readiness is that external stimuli impinging on highly excitable motor structures at a sufficiently high level in the hierarchy of the motor pathway are able to trigger the whole set of motor commands for execution of the fully prepared voluntary ballistic reaction (Valls-Solé et al., 1999a).

The fact that the perception of the prepulse was not always conscious does not preclude the possibility that the subject actually reacts to it in a number of trials. Blumenthal and Goode (1991) demonstrated that, in certain instances, a low-intensity stimulus may elicit responses just as those elicited by a high-intensity stimulus, and Taylor and McCloskey (1990) showed that stimuli that do not reach consciousness can trigger preprogrammed movements. In a state of high preparation for movement execution, subjects may direct their attention to the sensory modality in which the imperative signal is expected, and inputs from other sensory channels may be regarded as irrelevant. The pathway of other sensory channels to the sensorimotor cortex are probably blocked (Brunia, 1993). Therefore, subjects might not have been conscious of the prepulse stimulus even though it could have had effects at a subcortical level. The variability of the effects of a prepulse stimulus shown by our results might have been due to a variable degree of motor preparation of our subjects in different trials.

The combination of an enhanced motor preparation and the gating of sensory channels is probably responsible for the main observation reported here, the fact that prepulse stimuli are inhibiting the startle reaction but they do not prevent the acceleration of the reaction time. Such dichotomy suggests that the startle reaction and the effects of a startling stimulus on reaction time are two separate events. Evidence for the dissociation of these two effects of a startle is also consistent with the prominent habituation of the startle reaction (Brown et al., 1991a), while the StartReact phenomenon shows markedly less habituation (Valls-Solé et al., 1997; Valldeoriola et al., 1998).

The excitability of the descending subcortical motor tracts activated by a SAS may be primed during motor preparation for execution of a ballistic movement. This may contribute to the lack of habituation, increased response size, and reaction time shortening effects already reported. However, priming is probably focused in the muscles selected by the commands of the motor program, probably including agonist and postural muscles alike (Brown et al., 1991b). Other muscles may retain the same level of reactivity to startle and prepulse stimuli as in resting conditions and,

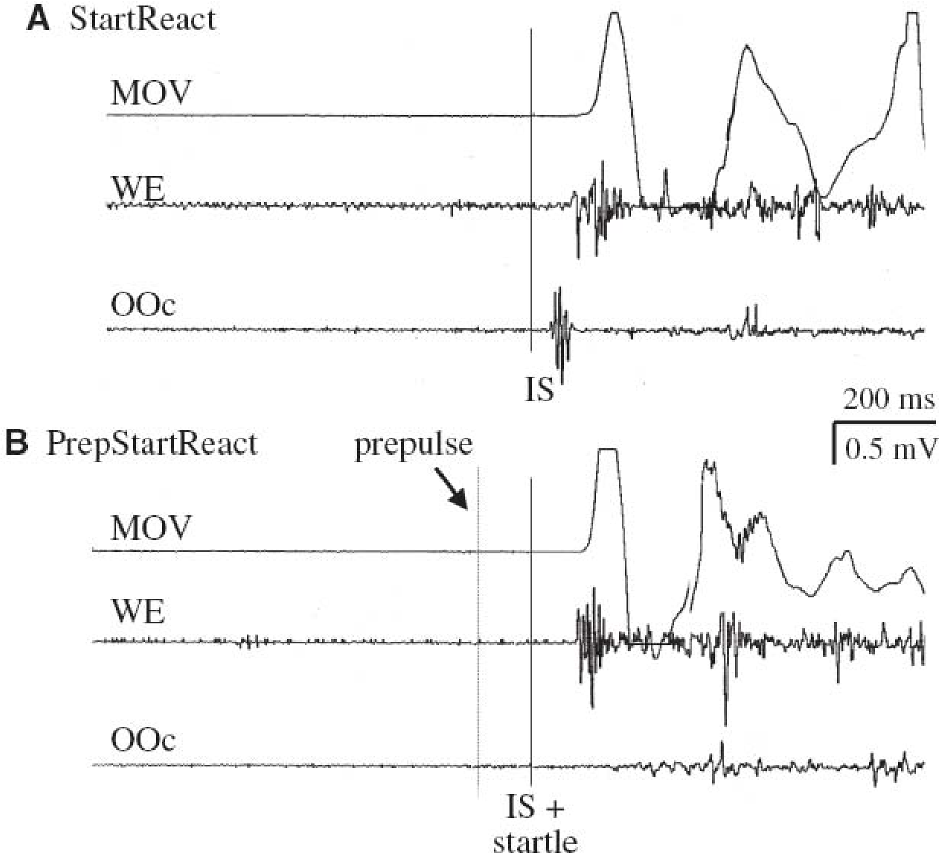


Fig. 4. Examples of a reaction time response, taken from the same subject as in Figs. 1 and 2, in the conditions StartReact (A) and PrepStartReact (B). Note the absence of the startle reaction in the orbicularis oculi in the condition PrepStartReact.

therefore, sustain the effects of the prepulse without the constraint imposed by the preparation-related excitability enhancement. Consistent with this idea, we saw absence of the startle reaction in orbicularis oculi and sternocleidomastoid muscles in PrepStartReact trials, because these muscles are not actually activated in the forearm reaction. Notably, Siegmund et al. (2001) were able to distinguish between the voluntary activity and the startle-related activity of the sternocleidomastoid muscle in a study of the StartReact phenomenon in that muscle. It would be interesting to measure whether prepulse inhibition also abolishes the startle-related activity in the sternocleidomastoid muscle, while still keeping the reaction time shortening effect, when this particular muscle is the primary mover (Siegmund et al., 2001).

5. Acknowledgements

This work was accomplished in part thanks to grant number V-2003-REDC06H –O from Instituto de Salud Carlos III.

References

Blumenthal, T.D. and Gescheider, G.A. (1987) Modification of the acoustic startle reflex by a tactile prepulse: the effects of stimulus onset asynchrony and prepulse intensity. Psychophysiology, 24: 320–327.

Blumenthal, T.D. and Goode, C.T. (1991) The startle eyeblink response to low intensity acoustic stimuli. Psychophysiology, 28: 296–307.

Brown, P., Rothwell, J.C., Thompson, P.D., Britton, T.C., Day, B.L. and Marsden, C.D. (1991a) New observations on the normal auditory startle reflex in man. Brain, 114: 1891–1902.

Brown, P., Day, B.L., Rothwell, J.C., Thompson, P.D. and Marsden, C.D. (1991b) The effect of posture on the normal and pathological auditory startle reflex. J. Neurol., Neurosurg. Psychiatr. 54: 892–897.

Brunia, C.H. (1993) Waiting in readiness: gating in attention and motor preparation. Psychophysiology, 30: 327–339.

Graham, F. (1975) The more or less startling effect of a weak prestimulation. Psychophysiology, 12: 238–248.

Henderson, L. and Dittrich, W.H. (1998) Preparing to react in the absence of uncertainty: I. New perspectives on simple reaction time. Br. J. Psychol., 89: 531–554.

Michie, P.T., Clarke, A.M., Sinden, J.D. and Glue, L.C.T. (1976) Reaction time and spinal excitability in a simple reaction time task. Physiol. Behav., 16: 311–315.

Pascual-Leone, A., Valls-Solé, J., Wassermann, E.M., Brasil-Neto, J.P., Cohen, L.G. and Hallett, M. (1992) Effects of focal transcranial magnetic stimulation on simple reaction time to acoustic, visual, and somatosensory stimuli. Brain, 115: 1045–1059.

Schieppati, M., Nardone, A. and Musazzi, M. (1986) Modulation of the Hoffmann reflex by rapid muscle contraction or release. Hum. Neurobiol., 5: 59-66.

Siegmund, G.P., Inglis, J.T. and Sanderson, D.J. (2001) Startle response of human neck muscles sculpted by readiness to perform ballistic head movements. J. Physiol., 535: 289–300.

Starr, A., Caramia, M., Zarola, F. and Rossini, P.M. (1988) Enhancement of motor cortical excitability in humans by non-invasive electrical stimulation appears prior to voluntary movement. Electroencephalogr. Clin. Neurophysiol., 70: 26–32.

Taylor, J.L. and McCloskey, D.I. (1990) Triggering of preprogrammed movements as reactions to masked stimuli. J. Neurophysiol., 63: 439–446.

Valldeoriola, F., Valls-Solé, J., Tolosa, E., Ventura, P.J., Nobbe, F.A. and Martí, M.J. (1998) The effects of a startling acoustic stimulus on reaction time in patients with different parkinsonian syndromes. Neurology, 51: 1315–1320.

Valls-Solé, J., Solé, A., Valldeoriola, F., Muñoz, E., Gonzalez, L.E. and Tolosa, E.S. (1995) Reaction time and acoustic startle in normal human subjects. Neurosci. Lett., 195: 97–100.

Valls-Solé, J., Valldeoriola, F., Tolosa, E. and Nobbe, F. (1997) Habituation of the auditory startle reaction is reduced during preparation for execution of a motor task in normal human subjects. Brain Res., 751: 155–159.

Valls-Solé, J., Rothwell, J.C., Goulart, F., Cossu, G. and Muñoz, J.E. (1999a) Patterned ballistic movements triggered by a startle in healthy humans. J. Physiol., 516: 931–938.

Valls-Solé, J., Valldeoriola, F., Molinuevo, J.L., Cossu, G. and Nobbe, F. (1999b) Prepulse modulation of the startle reaction and the blink reflex in normal human subjects. Exp. Brain Res., 129: 49–56.

IV. PUBLICACIÓN

Voluntary saccadic movements speeded up by a startle.

Experimental Brain Research. 2007; 177: 129-36.

7.4. El ESA induce un acortamiento marcado de la latencia de las sacadas dirigidas a una diana externa, sin que se modifiquen las características intrínsecas del movimiento ocular.

Esto sugiere que las sacadas están programadas principalmente en un nivel donde el ESA puede accionarlas. Esta acción puede utilizar un cortocircuito en el procesamiento sensorial pero esto no parece afectar la exactitud del movimiento al enfocar la diana. La ejecución involuntaria de movimientos sacádicos preparados no permite la modificación voluntaria de la direccionalidad de la mirada pero los resultados del experimento realizado indican que el tiempo requerido para el análisis de las señales incluidas en la diana es el mismo en condición basal y en la condición StartReact. Probablemente, los movimientos sacádicos pueden programarse de antemano si se sabe cuál será la diana. Esto es, por ejemplo, lo qué puede suceder al activar la reacción de escape o de lucha después de reconocer algunas características faciales en el caso de un agresor sospechado.

Exp Brain Res (2007) 177:129–136
DOI 10.1007/s00221-006-0659-4

RESEARCH ARTICLE

A startle speeds up the execution of externally guided saccades

**Juan M. Castellote · Hatice Kumru · Ana Queralt ·
Josep Valls-Solé**

Received: 1 June 2006 / Accepted: 26 July 2006 / Published online: 31 August 2006

Abstract The control of eye movements depends in part on subcortical motor centres. Gaze is often directed towards salient visual stimuli of our environment with no conscious voluntary commands. To further understand to what extent preprogrammed eye movements can be triggered subcortically, we carried out a study in normal volunteers to examine the effects of a startling auditory stimulus (SAS) on externally guided saccades. A peripheral visual cue was presented in the horizontal plane at a site distant 15° from the fixation point, and subjects were instructed to make a saccade to it. SAS was presented together with the peripheral visual cue in 20% of trials. To force rapid visual fixation at the end of the saccade, targets were loaded with a second cue, a small arrow pointing towards the right or the left (or a neutral sign), not distinguishable with peripheral vision. Subjects were requested to perform a flexion/extension wrist movement, according to the direction of the arrow (or not to move if the second cue was the neutral sign). SAS presented together with the visual target caused a significant shortening of the latency of saccadic movements. The wrist movements performed as a response to the second cue had similar reaction times regardless of whether the trial contained a SAS or not. Our results show that voluntary saccades to peripheral targets are speeded up by activation of the startle circuit, and that this effect does not cause a significant disturbance in the execution of simple in-target cues. These results suggest that subcortical structures play a main role in preparation of externally guided saccades.

Keywords Startle · Eye movements · Saccade · Electro-oculography · Reaction time

Introduction

A startling auditory stimulus (SAS) is known to induce a response in several muscles, known as the startle reaction (Landis and Hunt 1939; Wilkins et al. 1986; Brown et al. 1991a; Chokroverty et al. 1992; Kofler et al. 2001a, b). Reflex blinking is, by far, the most conspicuous involuntary movement produced by SAS-induced muscle contraction (Yeomans et al. 2002; Blumenthal et al. 2005; Flaten et al. 2005). Other movements may be elicited by SAS depending on factors such as body posture (Brown et al. 1991b), preparation for execution of a motor task (Valls-Solé et al. 1999), or other activities (Nieuwenhuijzen et al. 2000).

The oculomotor system has not been a frequent subject for research in the area of the startle. One of the reasons could be the interference of eyelid movements with the recording of eyeball movements (Gehricke et al. 2002; Rambold et al. 2005). During spontaneous, voluntary and reflex blinking or forced eyelid closure, the eyeball retracts 1 or 2 mm, due to co-contraction of all extraocular muscles (Evinger et al. 1984; Collewijn et al. 1985; Bour et al. 2000). Similar retraction can be expected from a blink-induced SAS. However, the

J. M. Castellote · A. Queralt
Facultad de Ciencias de la Actividad Física y el Deporte,
Universidad de Valencia, 46010 Valencia, Spain

H. Kumru · J. Valls-Solé (✉)
Unitat d'EMG, Servei de Neurologia, Hospital Clínic,
Universitat de Barcelona, IDIBAPS (Institut d'Investigació
Biomèdica August Pi i Sunyer), Barcelona 08036, Spain
e-mail: jvalls@clinic.ub.es

effects of a SAS on saccade preparation have not been explored so far. In limb muscles, delivering a SAS during preparation for execution of an intended movement shortens dramatically its onset latency (Valls-Solé et al. 1999; Carlsen et al. 2003, 2004). The nucleus reticularis pontis caudalis (nRPC) plays a crucial role for the generation of the startle response (Leintner et al. 1980; Davis et al. 1982; Brown et al. 1991a). The premotor burst neurons for horizontal saccades in man were found to lie in the medial part of the nRPC (Horn et al. 1995). The superior colliculus (SC) has well-known connections with the nRPC (Isa and Naito 1995; Zhao and Davis 2004). Therefore, we considered the possibility that SAS may have also an effect on saccades. Our first objective was to examine the effects of SAS on eye movements during gaze fixation and preparation for the execution of externally guided saccades. Our second objective was to examine the accuracy of saccades made with and without accompanying SAS by means of evaluating the reaction time and correctness of the responses to a secondary instruction built into the saccade target.

Subjects

The experiments were conducted in 18 healthy subjects (seven females and 11 males, aged 20–54 years). They all gave their informed consent for the experiments that were approved by the local Ethics Committee. All subjects were reportedly right-handed and used their right eye as the preferred one for focussing their vision. All had normal or corrected-to-normal vision and were free from any neurological deficits that could affect vision, eye, or hand movements.

Experimental setup and recording

Subjects sat on a chair adjusted to a comfortable height, with their chin resting on a head movement restrainer attached to a table. Room lights were dimmed. Vertical and horizontal eye movements were monitored with surface electrodes for electro-oculography (EOG) attached at all four poles of the right orbit (Heide et al. 1999). The active electrode for vertical movements was attached to the lower orbital rim, while the active electrode for horizontal movements was placed over the external orbital rim. We also recorded the EMG activity from the sternocleidomastoid muscles (SCM) with surface electrodes attached to the skin overlying the bulk of the muscles. The subject's forearm and hand were firmly attached to two joined metallic platforms in such a way that the wrist had only one degree of freedom for flexo-extension movements. A potentiometer, built in the hinge joining forearm and hand platforms, was used to monitor the wrist joint position signal. All bioelectric signals were recorded with, and temporarily stored on, a conventional electromyograph (MYSTRO5Plus; Oxford Medical Instruments, Surrey, UK). The bandpass frequency filters for eye and hand movements were 0.1–20 Hz, whereas the EMG of the SCM was recorded with a bandpass of 50–1,000 Hz. Eye movement towards the active electrode and wrist flexion movement were represented as negative-going deviations of the baseline. A circle of 2 cm diameter served as the fixation point for the subject's right eye.

Visual cue

A computer monitor, installed within the subject's right visual field, was used to trigger the visual stimulus used as target. This was a 5 cm^2 white square, shown on a blank screen. The target, generated when one of the experimenters pressed a computer key, was always presented on the same spot, at an angular distance of 15° to the right of the gaze fixation point.

The target contained an in-target imperative signal (IS) intended for the subjects to make a secondary task after they focussed their gaze on the target and perceived the IS. This consisted of a 1 cm long arrowhead pointing to the left (left filled triangle) or to the right (right filled triangle), or a square (filled square). These signals appeared at random with a rate of 40% for each arrow head and 20% for the square and required the subject to make a ballistic right hand movement to the left (flexion) or to the right (extension) depending on whether the arrow pointed to the left or to the right, or not to move if the symbol was a square. Symbols were made to appear together with the target.

Startling auditory stimulus

Startling auditory stimulus consisted in a loud sound generated by discharging the coil of a magnetic stimulator over a metallic platform. The sound produced in this way has an intensity of 130 dB SPL, when measured at a distance of 1 m from the source with a Brüel and Kjaer Impulse Precision Sound Level Meter type 2204 and is effective in inducing a startle reaction (Valls-Solé et al. 1999). Subjects were given a demonstration of the SAS before beginning the recording session in order to avoid unsuitable reactions due to a surprise effect.

Instructions and general procedure

All experimental sessions began with explaining the tests to the subjects making sure that they understood them correctly and with demonstrating the SAS. After recording electrodes were put on, subjects were instructed to stay relaxed and follow the instructions. We started by recording five calibration trials in which subjects were requested to perform a fast eye movement along the 15° distance from the gaze fixation point to the target. Subjects were allowed to practice a sufficient number of trials to become accustomed to the task. Data collection began when subjects felt confident with their performance, usually after 4–6 trials. Subjects were instructed to look towards the gaze fixation point, and a verbal forewarning was issued for them to be prepared to make a saccadic movement at the perception of the target on their right peripheral visual field. In all instances, the initial gaze fixation point remained present. Subjects were also instructed to be prepared to react by performing a rapid wrist flexion or extension movement when they perceived the in-target symbol. We warned our subjects of the possibility that a SAS could be present in some of the trials, and encouraged them to be prepared to react to the visual cue regardless of the interference of the acoustic stimuli. No other interventions were made in control trials. In test trials, interspersed randomly, the presentation of the target was accompanied by the presentation of SAS. This was made possible by sending an external trigger signal from the Mystro5Plus electromyograph to the magnetic stimulator at the same time when the target was shown on the screen. In order to maintain the subject's attention, SAS was applied on its own in three trials interspersed among control and test trials. In these SAS-alone trials no verbal forewarning or visual cue were presented.

Trials in which subjects began an eye movement during the 1 s period before target presentation were excluded. We also excluded trials in which subjects made a precipitated hand movement (before the end of the saccade) or moved the hand in the wrong direction. In these cases, trials were counted as errors and repeated on-line until we ended up with a total of 50 saccade trials per subject. These included 40 control trials and ten test trials for each condition. The in-target IS requiring wrist flexion or extension was presented in 20 trials each, while the ten remaining trials contained the IS requiring not to react (catch trials). In the ten test trials, the instructions were flexion in four, extension in four and not to move in two.

Data analysis

We measured the signals generated by the EOG and the wrist movement transducer. In SAS-alone trials, we calculated EOG vertical and horizontal onset latencies. In saccade trials, we measured for each subject the following variables, separately for control and test trials: saccade onset, determined as the latency of the first deviation of the baseline in the EOG recording for horizontal eye movements as previously described (Gribble et al. 2002); saccade end, determined as the time difference in ms between the presentation of the target and the end of the horizontal saccade in the EOG; saccade duration, determined as the time difference in ms between saccade end and saccade onset; saccade amplitude, determined as the amplitude of the linear displacement in the EOG, expressed in degrees after initial calibration of the eye movement (mean displacement in the calibration trials = 15°); hand movement reaction time, determined as the time difference between saccade end and the first consistent deviation from the baseline of the hand movement transducer signal. SCM–EMG was measured in test trials. The number of trials in which subjects made an error in the direction of hand movement (HM) (excluded from the main analysis) was expressed in percentage of the total number of trials. We included in the same determination the trials in which movements were made when the subject did not have to move.

We calculated the mean and SD for all parameters for each subject, grouped for type of trial. Statistical comparisons were done with one-factor (control versus test) repeated measures ANOVA, the dependent variables being saccade onset, saccade end, saccade amplitude, and hand movement reaction time.

Results

In SAS-alone trials, subjects reacted with a blink reflex that was recorded as a downward deflection in the vertical EOG at a mean onset latency of 48.6 ms (SD = 2.5 ms). No significant change was observed in the horizontal EOG (Fig. 1).

In control trials, the horizontal EOG signals accompanying saccades were recorded as a single straight

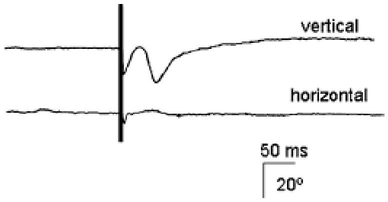


Fig. 1 Electro-oculogram from a representative subject showing the response to a startling auditory stimulus (*SAS*) applied with no preparation (SAS-alone trial)

line, consisting of a sharp deviation from the baseline followed by a slow return (Fig. 2a). No double saccades were observed in any trial. In test trials saccade onset was markedly shortened with respect to control trials, with no apparent changes in the latency of hand movement with respect to saccade end (Fig. 2b). Mean values are shown in Table 1 for all parameters measured in control and test trials. ANOVA showed that there were significant differences in saccade onset ($F = 39.6$; $p < 0.0001$) and saccade end ($F = 29.9$; $p < 0.0001$). No significant differences were found for saccade duration ($F = 0.001$; $p = 0.9$), saccade amplitude ($F = 0.2$; $p = 0.7$), or hand movement ($F = 1.60$, $p = 0.2$). The burst of EMG activity in the SCM was present in all test trials. The mean values for all individual trials pooled together were 46 ± 11 ms for onset latency and 2.1 ± 1.4 mV ms for response size. The large intra- and inter-individual variability in latency and amplitude of the response had a weak correlation with the percentage shortening of saccade onset latency for the same trial (Pearson's correlation coefficient of −0.56 for onset latency and +0.64 for size).

Errors in the direction of hand movement occurred in all types of trials, but their number was largely variable among individuals, ranging from 0 to 3 in control trials and 0–4 in test trials. The mean percentage of error trials was larger in test than in control trials (*t*-test; $p < 0.01$). The percentage of errors made in catch trials (included in the data above) was larger in test than in control trials (with 0–2 errors out of the eight catch trials per subject interspersed among the control trials and 0–2 errors out of the two catch trials interspersed among the test trials). Hand movement reaction time was largely variable among individuals in error trials. Mean hand movement reaction time in test trials with errors was 211.7 ms (SD = 79.7 ms). These figures were significantly shorter than the mean values reported for trials with no apparent errors in Table 1 (unpaired *t*-test, $p < 0.001$).

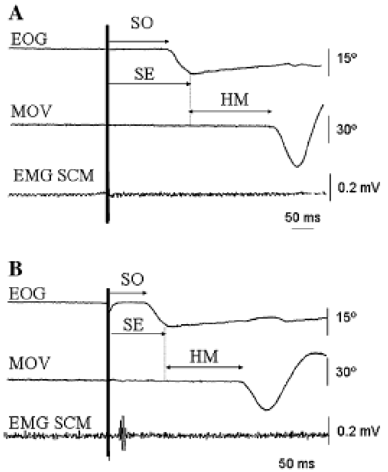


Fig. 2 The graphs are examples of recordings in control (**a**) and test (**b**) trials for saccade movements. They show a horizontal saccadic movement (*upper trace*), a hand movement (*middle trace*), and the EMG activity picked up from the left SCM (*lower trace*). Note the shortening of latency of the saccadic movement with no apparent changes in the latency of the hand movement with respect to the end of the saccade

Discussion

In this study we analysed the effects of a startle on the oculomotor system in preparation for a movement in an attempt to further understand the relationship between the startle reaction and the subcortical centres of eye movement control. Our results can be summarized in two main observations: (1) There was a speeding up execution of prepared saccadic movements made to a peripheral target when SAS was applied together with the visual target. (2) There were no differences between control and test trials in the execution of the secondary task, which instructions were only detected after saccade end and perception of target contents. In the following discussion, we will focus on how these results can be explained in the light of known physiology of eye movements and motor preparation.

Effects of startling auditory stimulus on saccade execution

Descriptions of movements observed in the startle reaction do not usually include ocular movements (Wilkins et al. 1986; Brown et al. 1991a; Chokroverty

Table 1 Mean data in control and test trials

	Saccades		
	Control	Test	%
SO	239.4 (72.5)	159.4 (25.9)	66.6
SE	341.8 (68.9)	256.4 (47.1)	75.0
SD	101.6 (14.3)	96.8 (15.6)	95.3
SA	15.0 (0.8)	14.9 (0.9)	99.3
HM	331.7 (51.0)	310.3 (57.2)	93.5

Numbers are the mean and 1 SD value (within parenthesis) of each of the measurements listed in the left column

SO saccade onset in ms, *SE* saccade end in ms, *SD* saccade duration in ms, *SA* saccade amplitude in degrees, *HM* hand movement reaction time in ms et al. 1992). Small and brief eye movements have been described with spontaneous blinking (Evinger et al. 1984) and also with reflex blinking to trigeminal nerve stimulation (Bour et al. 2000). Since blinking was indeed elicited by SAS in our subjects, we expected some small eye movements to occur. However, no eye movements were noticed in our study in the SAS-alone trials. It is possible that the superimposition of eyelid movement with the relatively small eye displacement of 1–2 mm (Bour et al. 2000) prevented the observation of any eye movement in the EOG. Recording the eye movements that could have been induced by the SAS in conditions of no preparation for a saccadic movement is an unresolved issue that would require a specific movement recording system. However, our results from the SAS-alone trials suggest that a SAS delivered with no preparation does not trigger an eye movement that could interfere with the recordings during execution of horizontal saccades. Furthermore, the observation of no differences regarding saccade duration and trajectory between control and test trials indicate that SAS did not induce significant changes on the intrinsic characteristics of the saccades.

It could be argued that the shortening of saccade onset in our subjects was related to the startle-induced reflex blinking. Gandhi and Bonadonna (2005) examined whether cessation of firing in omnipause neurons during blinking was sufficient to trigger saccades. In their study, when corneal air-puffs were delivered shortly after the cue to initiate movement, saccades occurred earlier in a linear relationship with blinking. However, this was not the case when reflex blinking overlapped with the cue (Gandhi and Bonadonna 2005). In a study in monkeys, Goossens and Van Opstal (2000) showed that reflex blinks induced by corneal air-puffs at onset of saccade dramatically changed the trajectory of the saccades. Modifications of saccades with blinking have also been described but with voluntary blinking (Rottach et al. 1998; Rambold et al. 2002). However, these observations do not apply to the results of our study. Blinking in our subjects occurred as a lateral manifestation of the startle reflex and caused no interference with the execution of the horizontal saccades. We believe that the saccade latency shortening observed in our study is independent of the startle-induced reflex blinking. However, it is possible that blinking contributed to accelerate saccade onset by disengaging gaze fixation.

Connections have been described between the reticular formation and the SC that could actually mediate the startle-induced saccade latency shortening by impinging on the executional centres for eye movements (Smit et al. 2005). This effect has been observed with limb movements in experiments involving simple reaction time tasks (Valls-Sole et al. 1999; Carlsen et al. 2003, 2004). In those instances, reaction time was so short that subcortical triggering of the motor program was favoured over cortical processing of sensory inputs (Valls-Sole et al. 1999). As with limb movements, the latency of eye movements performed in trials containing SAS was shortened with respect to control trials. Although the latency of saccade onset in test trials allows for the possibility of cortical processing, we think that the preparation of subcortical motor circuits plays the most important role for the shortening of saccade onset latency. Indeed, a high degree of motor preparation is an important requirement for the StartReact phenomenon to occur (Valls-Sole 2004; Kumru and Valls-Sole 2006). This may be the reason why the StartReact effect is less marked in choice than in simple reaction time paradigms (Valls-Sole 2004) and the startle reaction is larger in forced choice reaction time than in Go-noGo paradigms (Kumru et al. 2006). In our subjects, the percentage saccade onset latency shortening varied according to the size of the SCM burst, which is another argument favouring the relationship between the degree of subcortical motor preparation and the actual reaction time. We think that commands required for execution of a saccade are highly prepared and stored at a subcortical level, ready to be launched by an appropriate external trigger, as it is the case in most SRT paradigms (Henderson and Dittrich 1998).

Intentional visually guided saccades are likely generated in the frontal eye field (FEF), which neurons project not only to the deep layers of the SC but also to the pre-motor reticular formation of the brainstem (Pierrot-Deseilligny et al. 1995). In our paradigm, subjects had to perform an active disengagement from the fixation point before the saccade. Probably this involves cessation of activity in fixation-related cortical neurons of the FEF (Petit et al. 1995; Sommer and Wurtz 2000), de-activation of fixation neurons in the rostral SC (Gnadt et al. 1997), and dis-inhibition of saccade related neurons in SC (Munoz and Wurtz 1993; Munoz and Istvan 1998). It is possible that all mechanisms enabling fixation are interconnected, following a kind of corticotectal sequence that finalizes at the burst neurons of the brainstem reticular formation (Moschovakis 1996). If this is the case, external activation of the reticular formation could overcome the proposed steps and trigger the movement by actively disinhibiting the neurons in charge of movement execution. Premotor burst neurons of the brainstem reticular formation controlling horizontal saccades lie in the medial part of the nRPC (Horn et al. 1995), and a strong relationship between the nRPC and the SC has been thoroughly documented (Isa and Naito 1995; Zhao and Davis 2004).

Our data are consistent with the activation of a short-circuit at a site where the saccade is already fully programmed. Shortening of saccade onset latency takes place also in express saccades in paradigms making use of the gap effect (Munoz and Fecteau 2002; Coubard et al. 2004). Although the amount of shortening was significantly larger with the StartReact effect than with the gap effect, we should consider the mechanisms by which a saccade is speeded up in the gap effect in the discussion of possible explanations for our results (Sparks et al. 2000; Boulinguez et al. 2001). One of the opinions is that turning off the gaze fixation point causes disengagement of the fixation neurons of the SC (Munoz and Wurtz 1993; Moschovakis 1996). A similar disengagement from fixation could take place with reflex blinking occurring in the startle reaction or after startle-induced direct activation of the lateral portion of the SC, an area involved in coordination of eye and eyelid movements (Smit et al. 2005). Visually guided saccadic eye movements like those examined in our study were delayed after transcranial cortical magnetic stimulation (Priori et al. 1993), an observation pointing at a transient interruption of cerebral motor processing. However, the same stimulus did not affect express saccades which are thought to be mediated by subcortical structures without involvement of the cortex.

In our experiment, SAS could have induced a bypass of the cortical output to brainstem centres. The SC contains the structures that would make the generation of speeded-up saccades possible. A gradual build-up in activity takes place in neurons of the deep layers of the SC before execution of a saccade (Isa 2002). If activity in the deep layers of the SC is low when the visual input reaches the superficial layers, the visual input is relayed through cortical structures. However, in case of a high level of activity in the deep layers of the SC, inputs on the superficial layers could activate the deep layers and produce an express saccade (Isa 2002). A strong connectivity between superficial and deep layers has been already suggested by Behan and Appell (1992), Lee et al. (1997), and Doubell et al. (2003). These authors showed a strong staining of neurons of the deep layers of the SC after injection of a tracer in the neurons of the superficial layers. A similar mechanism could take place with auditory stimuli. It has been recently reported that, in monkeys, combined audiovisual stimuli induce reduced saccadic reaction times in comparison to unimodal stimuli (Bell et al. 2005). This was explained by an increase in premotor activity in neurons of the intermediate/deep layers of the SC, which should have the capability of integrating converging sensory inputs to influence the time of saccade initiation. Eye movement-related responses have been found in neurons of the ventral part of the human subthalamic nucleus in one experiment performed with the electrodes inserted for deep brain stimulation in eight patients with Parkinson's disease (Fawcett et al. 2005). The role of such connections between the subthalamic nucleus and eye movements is not known but one of the possibilities is that they subserve a circuit projecting from the caudate to the substantia nigra pars reticulata (SNpr). The SNpr is known to exert a tonic inhibitory action on neurons of the intermediate layer of the SC, which is conveniently removed prior to saccade onset (Matsumura et al. 1992; Hikosaka et al. 2000). The activity found in the subthalamic nucleus could be modulating the output of the SNpr towards the SC as a manifestation of the basal ganglia control of eye and eyelid movements (Moschovakis 1996; Gnadt et al. 1997).

Accuracy of saccadic movements performed in startling auditory stimulus trials

The question of whether the movement executed is actually the movement intended is relevant not only for the physiology of the StartReact effect but also to provide further light on the relationship between movement and perception. Eye movements hold special characteristics that make them appropriate for the study of target accuracy. Therefore, by requesting the subjects to make a hand movement according to the in-target instructions, we aimed at finding out whether the endpoint of the horizontal saccade performed in test trials was modified or not with respect to a baseline condition and whether or not visual perception was delayed after SAS. The fact that the hand reaction time was similar in our subjects in control and test trials suggests that their perception after the saccadic movement was similar in both conditions, the only difference being the shorter onset and end of the saccade in test trials. This in turn indicates that the amplitude of the saccade should have been fully programmed at the level where the SAS activated the system. Our results indicate that the motor commands required for the execution of a saccade are already represented in the reticular formation at the time of presentation of the IS.

Errors were seen in both conditions, although they were more frequent in SAS trials. The error trials had a shorter HM onset than non-error trials. This is probably the consequence of movement precipitation, an effect that can be often seen in choice reaction time task paradigms (Valls-Solé 2004). We think that some of our subjects prepared the wrist motor set largely in advance for a rapid performance and, therefore, precipitation occurred as a consequence of excessive preparedness. It has generally been held that motor preparation does not occur in choice reaction time tasks (Frith and Done 1986; Carlsen et al. 2004). However, our findings suggest that subjects may prepare a response that they are likely predicting. Predictive preparation could form an optimal strategy for rapid responding, as the process of building up an unprepared response may be slower and more effortful than inhibiting a motor drive that is already prepared (Henderson and Dittrich 1998).

In conclusion, the fact that SAS induces a dramatic shortening of onset latency of externally guided saccades without modifying the intrinsic characteristics of the ocular movement suggests that saccades are mainly programmed at a level where SAS can trigger them. Such triggering may use a short-circuit bypassing some sensory processing but does not seem to affect the accuracy of target reaching. SAS-induced involuntary execution of prepared saccades does not allow for voluntary modification of gaze directionality but this does not seem to affect the time processing required for the analysis of the in-target signals.

References

Behan M, Appell PP (1992) Intrinsic circuitry in the cat superior colliculus: projections from the superficial layers. J Comp Neurol 315:230–243

Bell AH, Meredith MA, Van Opstal AJ, Munoz DP (2005) Crossmodal integration in the primate superior colliculus underlying the preparation and initiation of saccadic eye movements. J Neurophysiol 93:3659–3673

Blumenthal TD, Cuthbert BN, Filion DL, Hackley S, Lipp OV, Van Boxtel A (2005) Committee report: guidelines for human startle eyeblink electromyographic studies. Psychophysiology 42:1–15

Boulinguez P, Blouin J, Nougier V (2001) The gap effect for eye and hand movements in double-step pointing. Exp Brain Res 138:352–358

Bour LJ, Aramideh M, Ongerboer DE, Visser BW (2000) Neurophysiological aspects of eye and eyelid movements during blinking in humans. J Neurophysiol 83:166–176

Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD (1991a) New observations on the normal auditory startle reflex in man. Brain 114:1891–1902

Brown P, Day BL, Rothwell JC, Thompson PD, Marsden CD (1991b) The effect of posture on the normal and pathological auditory startle reflex. J Neurol Neurosurg Psychiatry 54:892–897

Carlsen AN, Hunt MA, Inglis JT, Sanderson DJ, Chua R (2003) Altered triggering of a prepared movement by a startling stimulus. J Neurophysiol 89:1857–1863

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004) Prepared movements are elicited early by startle. J Motor Behav 36:253–264

Chokroverty S, Walczak T, Hening W (1992) Human startle reflex: technique and criteria for abnormal response. Electroencephalogr Clin Neurophysiol 85:236–242

Collewijn H, Van Der Steen J, Steinman RM (1985) Human eye movements associated with blinks and prolonged eye closure. J Neurophysiol 54:11–27

Coubard O, Daunys G, Kapoula Z (2004) Gap effects on saccade and vergence latency. Exp Brain Res 154:368–381

Davis M, Gendelman DS, Tishler MD, Gendelman PM (1982) A primary acoustic startle circuit: lesion and stimulation studies. J Neurosci 2:791–805

Doubell TP, Skaliora I, Baron J, King AJ (2003) Functional connectivity between the superficial and deeper layers of the superior colliculus: an anatomical substrate for sensorimotor integration. J Neurosci 23:6596–6607

Evinger C, Shaw MD, Peck CK, Manning KA, Baker K (1984) Blinking and associated eye movements in human, guinea pig and rabbits. J Neurophysiol 52:323–329

Fawcett AP, Dostrovsky JO, Lozano AM, Hutchison WD (2005) Eye movement-related responses of neurons in human subthalamic nucleus. Exp Brain Res 162:357–365

Flaten MA, Nordmark E, Elden A (2005) Effects of background noise on the human startle reflex and prepulse inhibition. Psychophysiology 42:298–305

Frith CD, Done DJ (1986) Routes to action in reaction time tasks. Psychol Res 48:169–177

Gandhi NJ, Bonadonna DK (2005) Temporal interactions of airpuff-evoked blinks and saccadic eye movements: insights into motor preparation. J Neurophysiol 93:1718–1729

Gehricke JG, Ornitz EM, Siddarth P (2002) Differentiating between reflex and spontaneous blinks using simultaneous recording of the orbicularis oculi electromyogram and the electro-oculogram in startle research. Int J Psychophysiol 44:261–268

Gnadt JW, Lu SM, Breznen B, Basso MA, Henriquez VM, Evinger C (1997) Influence of the superior colliculus on the primate blink reflex. Exp Brain Res 116:389–398

Goossens HH, Van Opstal AJ (2000) Blink-perturbed saccades in monkey. I. Behavioral analysis. J Neurophysiol 83:3411–3429

Gribble PL, Everling S, Ford K, Mattar A (2002) Hand-eye coordination for rapid pointing movements. Arm movement direction and distance are specified prior to saccade onset. Exp Brain Res 145:372–382

Heide W, Koenig E, Trillenberg P, Kömpf D, Zee DS (1999) Electrooculography: technical standards and applications. Electroencephalogr Clin Neurophysiol Suppl 52:223–240

Henderson L, Dittrich WH (1998) Preparing to react in the absence of uncertainty: I. New perspectives on simple reaction time. Br J Psychol 89:531–554

Hikosaka O, Takikawa Y, Kawagoe R (2000) Role of the basal ganglia in the control of purposive saccadic eye movements. Physiol Rev 80:953–978

Horn AK, Buttner-Ennever JA, Suzuki Y, Henn V (1995) Histological identification of premotor neurons for horizontal saccades in monkey and man by parvalbumin immunostaining. J Comp Neurol 359:350–363

Isa T (2002) Intrinsic processing in the mammalian superior colliculus. Curr Opin Neurobiol 12:668–677

Isa T, Naito K (1995) Activity of neurons in the medial pontomedullary reticular formation during orienting movements in alert head-free cats. J Neurophysiol 74:73–95

Kofler M, Muller J, Reggiani L, Valls-Sole J (2001a) Influence of gender on auditory startle responses. Brain Res 921:206–210

Kofler M, Muller J, Reggiani L, Valls-Sole J (2001b) Influence of age on auditory startle responses in humans. Neurosci Lett 307:65–68

Kumru H, Valls-Sole J (2006) Excitability of the pathways mediating the startle reaction before execution of a voluntary movement. Exp Brain Res 169:427–432

Kumru H, Urra X, Compta Y, Castellote JM, Turbau J, Valls-Sole J (2006) Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks. Neurosci Lett (in press)

Landis C, Hunt WA (1939) The startle pattern. Farrar and Rinehart, New York

Lee PH, Helms MC, Augustine GJ, Hall WC (1997) Role of intrinsic synaptic circuitry in collicular sensorimotor integration. Proc Natl Acad Sci USA 94:13299–13304

Leintner DS, Powers AS, Hoffman HS (1980) The neural substrate of the startle response. Physiol Behav 25:291–297

Matsumura M, Kojima J, Gardiner TW, Hikosaka O (1992) Visual and oculomotor functions of monkey subthalamic nucleus. J Neurophysiol 67:1615–1632

Moschovakis AK (1996) The superior colliculus and eye movement control. Curr Opin Neurobiol 6:811–816

Munoz DP, Fecteau JH (2002) Vying for dominance: dynamic interactions control visual fixation and saccadic initiation in the superior colliculus. Prog Brain Res 140:3–19

Munoz DP, Istvan PJ (1998) Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. J Neurophysiol 79:1193–1209

Munoz DP, Wurtz RH (1993) Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. J Neurophysiol 70:559–575

Nieuwenhuijzen PH, Schillings AM, Van Galen GP, Duysens J (2000) Modulation of the startle response during human gait. J Neurophysiol 84:65–74

Petit L, Tzourio N, Orssaud C, Pietrzyk U, Berthoz A, Mazoyer B (1995) Functional neuroanatomy of the human visual fixation system. Eur J Neurosci 7:169–174

Pierrot-Deseilligny C, Rivaud S, Gaymard B, Muri R, Vermersch AI (1995) Cortical control of saccades. Ann Neurol 37:557–567

Priori A, Berardelli A, Rothwell JC, Day BL, Marsden CD (1993) Some saccadic eye movements can be delayed by transcranial magnetic stimulation of the cerebral cortex in man. Brain 116:355–367

Rambold H, Sprenger A, Helmchen C (2002) Effects of voluntary blinks on saccades, vergence eye movements, and saccade-vergence interactions in humans. J Neurophysiol 88:1220–1233

Rambold H, El Baz I, Helmchen C (2005) Effect of blinks on saccades before smooth-pursuit eye-movement initiation. Ann NY Acad Sci 1039:563–566

Rottach KG, Das VE, Wohlgemuth W, Zivotofsky AZ, Leigh RJ (1998) Properties of horizontal saccades accompanied by blinks. J Neurophysiol 79:2895–2902

Smit AE, Zerari-Mailly F, Buisseret P, Buisseret-Delmas C, Vanderwerf F (2005) Reticulo-collicular projections: a neuronal tracing study in the rat. Neurosci Lett 380:276–279

Sommer MA, Wurtz RH (2000) Composition and topographic organization of signals sent from the frontal eye field to the superior colliculus. J Neurophysiol 83:1979–2001

Sparks D, Rohrer WH, Zhang Y (2000) The role of the superior colliculus in saccade initiation: a study of express saccades and the gap effect. Vision Res 40:2763–2777

Valls-Sole J, Rothwell JC, Goulart F, Cossu G, Munoz E (1999) Patterned ballistic movements triggered by a startle in healthy humans. J Physiol 516:931–938

Valls-Sole J (2004) Contribution of subcortical motor pathways to the execution of ballistic movements. Suppl Clin Neurophysiol 57:554–562

Wilkins DE, Hallett M, Wess MM (1986) Audiogenic startle reflex of man and its relationship to startle syndromes. A review. Brain 109:561–573

Yeomans JS, Li L, Scott BW, Frankland PW (2002) Tactile, acoustic and vestibular systems sum to elicit the startle reflex. Neurosci Biobehav Rev 26:1–11

Zhao Z, Davis M (2004) Fear-potentiated startle in rats is mediated by neurons in the deep layers of the superior colliculus/deep mesencephalic nucleus of the rostral midbrain through the glutamate non-NMDA receptors. J Neurosci 24:10326–10334

V. PUBLICACIÓN

Unilateral reaction time task is delayed during contralateral movements.

Experimental Brain Research. 2007;181:469-75.

7.5. La preparación subcortical motora se reduce significativamente durante la ejecución de otro movimiento voluntario. La ejecución de movimientos oscilatorios rítmicos con una extremidad interfiere en la ejecución de movimientos balísticos con el miembro contralateral. Esto fue observado tanto en ensayos conteniendo un ESA como en aquellos en que no existía ESA.

Exp Brain Res (2007) 181:469–475
DOI 10.1007/s00221-007-0944-x

RESEARCH ARTICLE

Unilateral reaction time task is delayed during contralateral movements

**Maike Begeman · Hatice Kumru ·
Klaus Leenders · Josep Valls-Sole**

Received: 17 January 2007 / Accepted: 27 March 2007 / Published online: 19 April 2007

Abstract Performing unlearned unimanual tasks when simultaneously carrying out another task with the contralateral hand is known to be difficult. The dual task interference theory predicts that reaction time will be delayed if the investigated task is performed in the course of ongoing contralateral movements. Ballistic movements can be performed at maximal speed in simple reaction time (SRT) experiments when subjects have adequately prepared the motor system needed for movement execution. When fully prepared, activation of subcortical motor pathways by a startling auditory stimulus (SAS) triggers the whole reaction. In this study, we have examined dual task interference with reaction time in eight healthy volunteers. They were presented with a visual imperative signal to perform unilateral SRT either in a baseline condition (control trials) or while carrying out contralateral rhythmic oscillatory movements (test trials). A SAS was introduced in 25% of the trials in both conditions. SRT was significantly delayed in the interference test trial when compared to control trials either with or without SAS ($P < 0.001$). Control and test trials with SAS were significantly faster than those without SAS in both conditions ($P < 0.001$). However, there were no significant differences in the percentage SRT shortening induced by SAS or in the percentage SRT delay observed in the test trials. Our results suggest that performing rhythmic oscillatory movements with one limb slows SRT in the contralateral limb and that this effect is likely related to motor preparation changes. The effect described here can be of interest for physiological studies of interlimb coordination and the mechanisms underlying the dual task interference phenomenon.

Keywords Ballistic movement · Dual task interference · Motor preparation · Startling auditory stimulus

Introduction

Attempting to perform a unimanual task when simultaneously carrying out voluntary movements with the contralateral hand is a useful paradigm for the study of the dual task interference effect (Pashler 1994; Herath et al. 2001). In such conditions, the performance of one of the actions is typically impaired (Geurts et al. 1991; Lundin-Olsson et al. 1997; Mulder et al. 2002; Kumru et al. 2004; Jiang 2004). One example of dual task interference is the transient alteration of unilateral rhythmic oscillatory movements by performing a contralateral ballistic movement (Kumru et al. 2004). The opposite effects, i.e. those of rhythmic movements on the speed of a unilateral ballistic movement in a simple reaction time task paradigm (SRT), have been studied only scarcely (Buenaventura and Sarkin 1996; Castellote et al. 2004).

The physiological mechanisms underlying dual task interference are not completely understood. Executing a

---

M. Begeman · J. Valls-Sole
Unitat d'EMG, Servei de Neurologia,
Hospital Clinic, Facultad de Medicina,
IDIBAPS (Institut d'Investigació Biomèdica August Pi i Sunyer),
Universitat de Barcelona, Barcelona, Spain

H. Kumru (✉)
Instituto Guttmann,
Hospital de Neurorehabilitación, Camí de Can Rutí s/n,
08916 Badalona, Barcelona Spain
e-mail: hkumru@guttmann.com

K. Leenders
Department of Neurology,
University Medical Centre Groningen (UMCG),
University of Groningen, Groningen, The Netherlands

motor plan may involve issuing inhibitory commands to motor structures not involved in the voluntary action (Gerloff et al. 1998; Kumru et al. 2004; Gorsler et al. 2004). Alternatively, dual task interference may be an expression of a central bottleneck process for response selection or task execution (Pashler 1994; Lien and Proctor 2002; Muller et al. 2004; Ulrich et al. 2006). If one of the actions involves reacting to a sensory signal, factors involving the sensory system have to be taken into account, including divided attention (Sakai et al. 2000; Herath et al. 2001; Fernandes et al. 2006). Probably, many mechanisms simultaneously contribute to dual task interference with varying degrees depending on the specific experimental paradigm.

Our main objective in the study presented here has been to investigate whether performance of a voluntary movement prevents subcortical motor structures from reaching the required degree of preparation for fast execution of a ballistic movement. The amount of motor preparation reached before perception of the imperative signal (IS) directly correlates with the speed of the reaction in SRT paradigms (Henderson and Dittrich 1998; Carlsen et al. 2006). One method to measure the excitability enhancement occurring in subcortical motor structures before movement execution is the StartReact effect, i.e. the subcortical triggering of a motor task when a startling auditory stimulus (SAS) is presented to a subject who is highly prepared to execute that motor task (Valls-Solé et al. 1999; Kumru and Valls-Sole 2006; Kumru et al. 2006; Carlsen et al. 2006). Therefore, we sought to improve our understanding of physiological mechanisms of motor control and, specifically, of some of the mechanisms underlying the dual task interference effect by studying how unilateral oscillatory movements affect contralateral SRT, the StartReact effect or both.

Methods

The study was carried out in eight healthy subjects, five men and three women, aged 25–35 years. Seven subjects were right handed and one was left handed. We included no persons with known bimanual skills such as musicians or artists. All subjects gave written informed consent for the study, which was approved by our local Ethics committee.

Stimulation and recording

Subjects faced a 14-inch computer monitor, situated at approximately 50 cm before the subjects' eyes. They were requested to react to a visual cue appearing in the computer's monitor. A 1 cm × 1 cm white cross was presented in the centre of an otherwise black screen, serving as the forewarning for the IS and as a gaze fixation point. The IS was a 5 cm × 5 cm that appeared after a variable period between 500 and 1,500 ms. One second after the appearance of the small cross on the computer screen, a pulse was generated by the computer to trigger the electromyograph (Neuropack 8, Nihon-Kohden, London).

A lineal accelerometer (model 348720; Bionic Ibérica S.A., Barcelona, Spain) was placed on the dorsum of each hand in the best position to record wrist oscillations and its changes before and during the tasks. The accelerometer recordings were low-pass filtered (0.1–10 Hz), digitized at a sampling rate of 200 Hz and stored on a personal computer equipped with the software package Acknowledge MP100 (Biopac Systems, Bionic Ibérica S.A., Barcelona). Individual recordings were classified according to condition for off-line analysis.

Startling auditory stimulus, applied in some trials as described under Sect. 'Experimental procedure', was produced by discharging the coil from a magnetic stimulator over a metallic platform. This produced a sound of an intensity of 130 dB sound pressure level, measured at a distance of 1 m from the source with a Brüel and Kjaer Impulse Precision Sound Level Meter type 2204. Such a procedure has been shown to be effective in inducing a startle reaction in most healthy subjects (Valls-Solé et al. 1999).

Experimental procedure

The subjects were sitting on a chair with their elbows supported by armrests and their hands relaxed and outstretched on top of a conveniently placed wooden surface, at approximately 30 cm distance from each other and 15 cm away from a 2 cm^2 button. They received full verbal instructions of the experiment. All trials began by asking the subject to pay attention to the computer's monitor and be ready to react. The task was to hit the button as fast as possible at the perception of the IS. The procedure involved two experimental conditions presented in a random order:

1. In the control condition, the subjects were requested to keep their hands in the resting position, on top of the wooden surface, until they performed the reaction.
2. In the test condition, subjects were requested to perform tremor-like rhythmic unilateral oscillatory wrist movements and carry out the same task as described above with the contralateral hand. We did not specify frequency or amplitude of the oscillatory movement, but requested to perform a smooth, consistent and rhythmic but comfortable wrist oscillation of more than 3 Hz, which could be maintained for extended periods of time.

Left and right hands were examined in a random order. For each condition, we collected a total of 20 trials for each hand. In 15 of them, we presented just the IS, while in the other five we presented the IS together with a SAS. The five trials containing SAS were intermingled with those containing no SAS in a random order. Additionally, we presented sham trials in which SAS was delivered while the subjects were either at rest or imitating tremor, but had not received any instructions regarding preparation for a reaction (no verbal commands for readiness, warning signal or IS). Two sham trials were presented for each condition. The subjects were allowed to practice to feel comfortable with the task. Trials were rejected on-line and repeated if subjects reacted before the IS or reacted late because of self-reported lack of attention.

Data reduction and analysis

We recorded periods of 4 s, which included 1,000 ms preceding the IS. We performed off-line analysis of the mean dominant frequency of the tremor-like oscillation in the pre-IS period using the Fast Fourier transform. Reaction time was measured as the latency in ms between the IS and the onset of accelerometric signal displacement in the reacting hand. Data for each condition were grouped for control and test trials with and without SAS. Therefore, we ended up with four groups of data: control trials with no SAS, control trials with SAS, test trials with no SAS and test trials with SAS.

For descriptive purposes, we calculated the mean and standard deviation values for each group of data. The individual's mean in the control trials with no SAS was assigned 100% and data for each trial in all groups were expressed as percentages. We used a two-factor ANOVA, one factor being the experimental condition (control vs test) and the other factor the presence or absence of SAS. Bonferroni's test was used for post-hoc analysis when significant differences were found. The Student's *t*-test was used for comparison of data from both sides. The level of statistical significance was set at $P < 0.05$.

Results

The experiments were completed without any difficulty by all subjects. The total duration of the experiment was about 1 h. There were no statistically significant differences in SRT in the control trials without SAS between the dominant and non-dominant hand (dominant hand 170.5 ± 12.1 ms; non-dominant hand: 172.1 ± 9.9 ms; *t*-test; P = 0.07). Therefore, we pooled data from both hands for further statistical comparisons.

In the test trials without SAS, the mean frequency of the oscillatory movement in the pre-IS period was 5.6 ± 0.5. As expected (Kumru et al. 2004), performing the ballistic reaction markedly modified the rhythmicity and consistency of the oscillations. The effect was variable among subjects, although all showed an amplitude decrement or transient stop of the oscillations in the majority of trials, with a mean latency of 138 ms (SD = 71 ms) and a mean duration of 314 ms (SD = 114 ms).

Startling auditory stimulus delivered at rest induced a slight wrist flexion movement in some subjects at a mean latency of 109 ms (SD = 21 ms). This was induced by the first SAS in almost all subjects and by the second SAS in only three subjects. When subjects were performing oscillatory movements to imitate tremor, the first SAS caused a slight decrease in the amplitude of the oscillatory movement (ranging from 8 to 18% of the initial amplitude) in some trials in five subjects. Neither any stop nor any other relevant change was induced by the second SAS in any of the subjects of our study.

The individual mean reaction time changes are depicted in Fig. 1 for the control and test trials with and without SAS. Table 1 shows the mean reaction time in absolute values and in percentage for the two conditions and the two types of trials. Statistical comparisons showed a significant effect of type of trial (ANOVA; $F = 146.3$; $P < 0.001$) and condition (ANOVA; $F = 46.4$; $P < 0.001$), but interaction between the two factors was not significant. The reaction time in the test trials was longer than that in the control trials, either with or without SAS. The mean percentage shortening induced by SAS was not significantly different when comparing control with test trials (66.6 ± 9.1% in control trials and 65.8 ± 10.2% in test trials). The percentage SRT lengthening induced by performing contralateral oscillatory movements was not significantly different when comparing trials with no SAS (124.9 ± 8.2%) and trials with SAS (126.5 ± 7.1%). Figure 2 shows examples of recordings from a representative subject for all four types of trials.

Discussion

There are two main results of our study: 1. Unilateral SRT is delayed when subjects perform oscillatory movements with the contralateral hand in comparison with the same task performed when subjects are at rest. 2. This effect occurs to a similar extent when SRT is speeded up in the context of a StartReact paradigm.

Delayed reaction time when performing contralateral oscillatory movements

It is common to experience difficulties when performing spatially or temporally differentiated tasks with both hands simultaneously (Buenaventura and Sarkin 1996; Klingberg and Roland 1997; Hazeltine et al. 2006; Matthews et al.

Fig. 1 Individual reaction time for each subject in both experimental conditions. Control: reaction time at rest (baseline condition). Test: reaction time during contralateral rhythmic oscillatory hand movements. *SAS*: startling acoustic stimulus

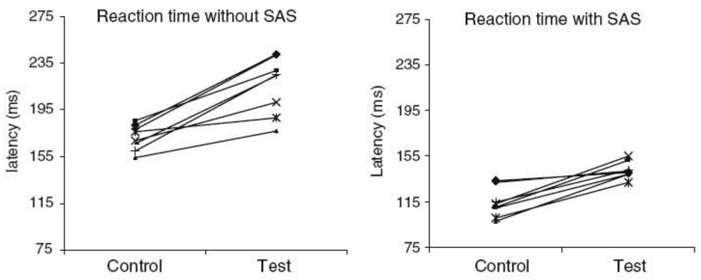


Table 1 Mean values of reaction time (standard deviation)

	Control-SRT (ms)	Test-SRT (ms)	Control-SRT (%)	Test-SRT (%)
No SAS	171.3 (11.0)	216.7 (24.8)	100.0 (6.4)	126.5 (11.4)
SAS	114.1 (12.3)	142.6 (7.6)	66.6 (10.8)	83.2 (5.3)

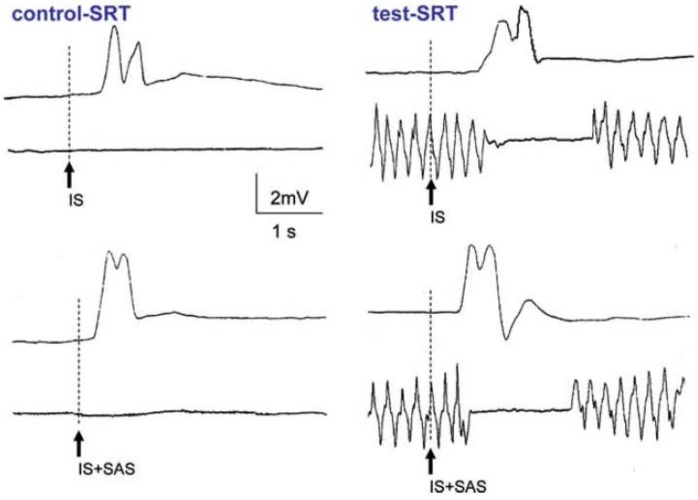
Values are the mean and one standard deviation (within parenthesis) for control and test trials with and without SAS. Values are given in ms and in percentage of the mean control trials. The percentage shortening of test trials with SAS compared to test trials without SAS is 65.8%

2006). This dual task interference has been used to demonstrate subtle motor dysfunctions in clinical practice, which have sometimes been reported with attractive names (Lundin-Olsson et al. 1997; de Hoon et al. 2003; Andersson et al. 2003; Hyndman and Ashburn 2004; Rochester et al. 2004; Hein et al. 2005). In an extensive review, Pashler (1994) reported delayed reaction time in the second task of a pair given in sequence, with a more marked delay when tasks had to be performed within short intervals. Surprisingly, however, unilateral SRT has been only scarcely considered as a probe for the interference effects. Buenaventura and Sarkin (1996) reported a delay in SRT when tapping with the contralateral hand, and Castellote et al. (2004) showed that unilateral SRT is also delayed when subjects perform their task on a background of ongoing slow oscillatory movements.

The physiological mechanisms underlying dual task interference in the context of SRT are not completely understood. Classically, a collision in perceptual processing of stimuli rather than impairment of motor preparation has been proposed. Recently, however, Obhi and Goodale (2005) showed evidence that interference occurs not only in stimulus processing, but also in motor preparation. Our findings suggest that there is indeed a lack of sufficient preparation within motor systems that could account for the delay in the execution of a motor task when performing oscillatory contralateral hand movements.

Excitability changes in cortical motor areas could provide an explanation for the findings of our study. Several authors have demonstrated an enhancement in the excitability of motor systems before and during the execution of a voluntary movement (Gerloff et al. 1998; Stinear et al. 2001; Sohn et al. 2003; McMillan et al. 2006). Excitability changes occur also in muscles not involved in the voluntary movement, with enhancement reported by some authors

Fig. 2 Selected recordings from a representative subject reacting with the right hand in control (*left*) and test (*right*) conditions. Trials with no SAS are displayed at the *top* of the figure, and those with SAS are displayed at the *bottom*. *IS* imperative signal, *SAS* startling acoustic stimulus



examining tonic contraction of homologous muscles (Stinear et al. 2001) and inhibition reported by authors examining phasic muscle contraction (Gerloff et al. 1998; Sohn et al. 2003). Our finding of a delay of test SRT compared to control SRT fits well with the observations reported by Sohn et al. (2003), who showed that phasic contraction of the first dorsal interosseous muscle caused inhibition of motor-evoked potentials elicited by single pulse TMS on the contralateral hand. Inhibition was not only directed towards the homologous muscles, but also involved a more diffuse area (Sohn et al. 2003). The degree of inhibition was larger for the distal and adjacent muscles than for the homologous and proximal muscles.

Divided attention, which is intrinsic to the execution of separated simultaneous bimanual tasks, can also provide an explanation for the interference effects reported here. Considering the fact that performance is better with attention to the task, it is not surprising that it gets worse when attention needs to be divided. Other studies also confirmed the role of divided attention in movement constraints (Herath et al. 2001; Mulder et al. 2002; Jiang 2004; Fernandes et al. 2006; Catena et al. 2007). Learning a new motor task is associated with progressive automatisms and reduced participation of cognitive areas of the brain (Puttemans et al. 2005). Mulder et al. (2002) showed that motor control of a task is most efficient when less cognitive involvement is needed. The more cognitive involvement is required in a task, the larger the interference produced by a concurrent attention-demanding task. Swinnen and Wenderoth (2004) showed that, when performing bimanual hand movements, the motor action is easier performed when it can be represented as a single task than when it is considered as two separate tasks. Divided attention is probably an important aspect of dual task interference, which may be relevant for the processing of inputs and transfer of motor programs to the execution channel for reaction time. However, it does not explain how interference is actually produced. Inhibition of contralateral motor tracts during an attention-demanding task is likely to play a role also. This could explain why reaction time is not only delayed during concurrent movements, but also during a mental task (Pashler 1994).

Effect of a SAS

A startling stimulus causes a significant shortening of the voluntary movement performed in SRT tasks when applied together with the IS or at a short interval afterwards (Valls-Sole et al. 1995; Valls-Solé et al. 1999; Siegmund et al. 2001; Carlsen et al. 2004; Kumru and Valls-Sole 2006). The movement to be performed in a SRT paradigm is thought to be prepared by subcortical structures activated directly by SAS (Valls-Solé et al. 1999; Carlsen et al. 2004). Speeding up of the SRT by SAS is likely to depend on the degree of subcortical motor preparation (Valls-Solé 2004). Recently, it has been demonstrated that the size of the startle reflex response changes in parallel with the percentage shortening of reaction time, an observation that further relates the StartReact effect with the excitability of subcortical motor structures activated by the SAS (Kumru and Valls-Sole 2006; Kumru et al. 2006; Carlsen et al. 2006). In the present study, we found that test trials with SAS were significantly delayed with respect to control trials with SAS. This suggests that the subjects were not able to fully engage their subcortical motor pathways in the reaction when performing contralateral oscillatory movements as when the contralateral hand was at rest. One likely explanation for the difference is that the subjects could not fully prepare their subcortical motor structures before IS detection. Lack of sufficient motor preparation is likely to be a manifestation of dual task interference. Therefore, our findings suggest that, in addition to many other physiological aspects underlying the dual task interference effect (Lien and Proctor 2002), limited preparation of subcortical motor structures contributes to the delay of SRT. This does not exclude the simultaneous contribution of other mechanisms, such as slowness of sensory processing because of divided attention and active inhibition linked to the issuing of motor commands, in the generation of the dual task interference effect.

An indirect consequence of our findings is that the StartReact effect may not entirely depend on the excitablity of the subcortical motor structures. Part of the effect may be due to the intersensory facilitation (Nickerson 1973; Carlsen et al. 2004; Kumru et al. 2006). Certainly, SAS delivered together with the IS is likely to induce intersensory facilitation of reaction time due to increased energy of the IS. However, the shortening observed with intersensory facilitation is no more than 50 ms (Nickerson 1973; Gielen et al. 1983). The shortening induced by SAS on SRT is usually larger than 50 ms, suggesting additional effects to those of intersensory facilitation. The electromyographic and kinematic characteristics of the movement performed with the StartReact phenomenon are not distorted with respect to those of the movement performed without interference of SAS (Valls-Solé et al. 1999). Therefore, the tracts activated by the SAS should be the ones used for execution of the motor commands. However, for this effect to take place, subjects have to have a high degree of preparation of their subcortical motor tracts (Kumru and Valls-Solé 2006; Carlsen et al. 2006). The amount of motor preparation in SRT can be very high since there is no need for sensory processing (Henderson and Dittrich 1998) and, consequently, the StartReact effect can lead to reaction times of values similar to those of the startle reaction. However, when performing unilateral oscillatory tremor-like movements, subjects may not be able to reach the same level of motor preparation as when they are at rest, which will lead to reduction of the StartReact effect. The degree of motor preparation of the subcortical motor tracts may control the extent of reaction time shortening induced by SAS, ranging from intersensory facilitation at one end, when full preparation is not possible, to a speed of execution similar to the startle reaction (StartReact effect) at the other end, when subjects have been able to reach full preparation.

In conclusion, our results show that performing oscillatory movements with one extremity interferes with the execution of ballistic movements with the contralateral one. In this condition, motor preparation of the subcortical motor tracts was insufficient to lead to the StartReact effect. This suggests that reduced motor preparation is an important mechanism to account for the delay in executing SRT when simultaneously performing contralateral movements. Our observations can be of interest for physiological studies of interlimb coordination and could contribute to improve our understanding of the mechanisms underlying the dual task interference phenomenon.

References

Andersson G, Hagman J, Talianzadeh R, Svedberg A, Larsen HC (2003) Dual-task study of cognitive and postural interference in patients with vestibular disorders. Otol Neurotol 24:289–293

Buenaventura RS, Sarkin AJ (1996) Reaction time crossover with an interfering task. Percept Mot Skills 82:867–871

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004) Can prepared responses be stored subcortically? Exp Brain Res 159:301–309

Carlsen AN, Dakin CJ, Chua R, Franks IM (2006) Startle produces early response latencies that are distinct from stimulus intensity effects. Exp Brain Res Jul 28 [Epub ahead of print]

Castellote JM, Valls-Sole J, Sanegre MT (2004) Ballistic reactions under different motor sets. Exp Brain Res 158:35–42

Catena RD, van Donkelaar P, Chou LS (2007) Cognitive task effects on gait stability following concussion. Exp Brain Res 176:23–31

de Hoon EW, Allum JH, Carpenter MG, Salis C, Bloem BR, Conzelmann M, Bischoff HA (2003) Quantitative assessment of the stops walking while talking test in the elderly. Arch Phys Med Rehabil 84:838–842

Fernandes MA, Pacurar A, Moscovitch M, Grady C (2006) Neural correlates of auditory recognition under full and divided attention in younger and older adults. Neuropsychologia 44:2452–2464

Gerloff C, Cohen LG, Floeter MK, Chen R, Corwell B, Hallett M (1998) Inhibitory influence of the ipsilateral motor cortex on responses to stimulation of the human cortex and pyramidal tract. J Physiol 510:249–259

Geurts ACH, Mulder T, Nienhuis B, Rijken RAJ (1991) Dual-task assessment of reorganization of postural control in persons with lower limb amputation. Arch Phys Med Rehabil 72:1059–1064

Gielen SC, Schmidt RA, Van den Heuvel PJ (1983) On the nature of intersensory facilitation of reaction time. Percept Psychophys 34:161–168

Gorsler A, Zittel S, Weiller C, Munchau A, Liepert J (2004) Modulation of motor cortex excitability induced by pinch grip repetition. J Neural Transm 111:1005–1016

Hazeltine E, Ruthruff E, Remington RW (2006) The role of input and output modality pairings in dual-task performance: evidence for content-dependent central interference. Cognit Psychol 52:291–345

Hein G, Schubert T, von Cramon DY (2005) Closed head injury and perceptual processing in dual-task situations. Exp Brain Res 160:223–234

Henderson L, Dittrich WH (1998) Preparing to react in the absence of uncertainty: I. New perspectives on simple reaction time. Br J Physiol 89:531–554

Herath P, Klingberg T, Young J, Amunts K, Roland P (2001) Neural correlates of dual task interference can be dissociated from those of divided attention: an fMRI study. Cereb Cortex 11:796–805

Hyndman D, Ashburn A (2004) Stops walking when talking as a predictor of falls in people with stroke living in the community. J Neurol Neurosurg Psychiatr 75:994–997

Jiang Y (2004) Resolving dual-task interference: an fMRI study. Neuroimage 22:748–754

Klingberg T, Roland PE (1997) Interference between two concurrent tasks is associated with activation of overlapping fields in the cortex. Brain Res Cogn Brain Res 6:1–8

Kumru H, Valls-Sole J (2006) Excitability of the pathways mediating the startle reaction before execution of a voluntary movement. Exp Brain Res 169:427–432

Kumru H, Valls-Solé J, Valldeoriola F, Marti MJ, Sanegre (2004) Transient arrest of psychogenic tremor induced by contralateral ballistic movements. Neurosci Lett 370:135–139

Kumru H, Urra X, Compta Y, Castellote JM, Turbau J, Valls-Solé J (2006) Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks. Neurosci Lett 406:66–70

Lien MC, Proctor RW (2002) Stimulus-response compatibility and psychological refractory period effects: implications for response selection. Psychon Bull Rev 9:212–238

Lundin-Olsson L, Nyberg L, Gustafson Y (1997) "Stops walking when talking" as a predictor of falls in elderly people. Lancet 349:617

Matthews A, Garry MI, Martin F, Summers J (2006) Neural correlates of performance trade-offs and dual-task interference in bimanual coordination: an ERP investigation. Neurosci Lett 400:172–176

McMillan S, Ivry RB, Byblow WD (2006) Corticomotor excitability during a choice-hand reaction time task. Exp Brain Res 172:230–245

Mulder T, Zijlstra W, Geurts A (2002) Assessment of motor recovery and decline. Gait Posture 16:198–210

Muller ML, Jennings JR, Redfern MS, Furman JM (2004) Effect of preparation on dual-task performance in postural control. J Mot Behav 36:137–146

Nickerson RS (1973) Intersensory facilitation of reaction time: energy summation or preparation enhancement?. Psychol Rev 80:489–509

Obhi SS, Goodale MA (2005) Bimanual interference in rapid discrete movements is task specific and occurs at multiple levels of processing. J Neurophysiol 94:1861–1868

Pashler H (1994) Dual-task interference in simple tasks: data and theory. Psychol Bull 116:220–244

Puttemans V, Wenderoth N, Swinnen SP (2005) Changes in brain activation during the acquisition of a multifrequency bimanual coordination task: from the cognitive stage to advanced levels of automaticity. J Neurosci 25(17):4270–4278

Rochester L, Hetherington V, Jones D, Nieuwboer A, Willems AM, Kwakkel G, Van Wegen E (2004) Attending to the task: interference effects of functional tasks on walking in Parkinson's disease and the roles of cognition, depression, fatigue, and balance. Arch Phys Med Rehabil 85:1578–1585

Sakai K, Hikosaka O, Takino R, Miyauchi S, Nielsen M, Tamada T (2000) What and when: parallel and convergent processing in motor control. J Neurosci 20:2691–2700

Siegmund GP, Inglis JT, Sanderson DJ (2001) Startle response of human neck muscles sculpted by readiness to perform ballistic head movements. J Physiol 535:289–300

Sohn YH, Jung HY, Kaelin-Lang A, Hallett M (2003) Excitability of the ipsilateral motor cortex during phasic voluntary hand movement. Exp Brain Res 148:176–185

Stinear CM, Walker KS, Byblow WD (2001) Symmetric facilitation between motor cortices during contraction of ipsilateral hand muscles. Exp Brain Res 139:101–105

Swinnen SP, Wenderoth N (2004) Two hands, one brain: cognitive neuroscience of bimanual skill. Trends Cogn Sci 8:18–25

Ulrich R, Fernandez SR, Jentzsch I, Rolke B, Schroter H, Leuthold H (2006) Motor limitation in dual-task processing under ballistic movement conditions. Psychol Sci 17(9):788–793

Valls-Solé J (2004) Contribution of subcortical motor pathways to the execution of ballistic movements. In: Hallett M, Phillips LH, Schomer DL, Massey JM (eds) Advances in clinical neurophysiology, vol 57. Elsevier, Amsterdam, pp 54–62

Valls-Sole J, Sole A, Valldeoriola F, Munoz E, Gonzalez LE, Tolosa ES (1995) Reaction time and acoustic startle in normal human subjects. Neurosci Lett 195:97–100

Valls-Solé J, Rothwell JC, Goulart F, Cossu G, Muñoz E (1999) Patterned ballistic movements triggered by a startle in healthy humans. J Physiol 516:931–938

Capitulo 8.- Publicaciones relacionadas con respuesta de sobresalto y tiempo de reacción

1. Kumru H, Summerfield C, Valldeoriola F, Valls-Sole J. Effects of Subthalamic nucleus stimulation on characteristics of EMG activity underlying reaction time in Parkinsons Disease. Movement Disorders 2004; 19: 94-100.
2. Kumru H, Valls-Sole J, Valldeoriola F, Marti MJ, Sanegre MT, Tolosa E. Transient arrest of psychogenic tremor induced by contralateral ballistic movements. Neurosci Lett. 2004; 370: 135-139.
3. Kumru H, Begeman M, Tolosa E, Valls-Sole J. Dual task interference in psychogenic tremor. Mov Disord. 2007; 22:2077-82.
4. Kumru H, Vidal J, Kofler M, Benito J, Garcia A, Valls-Solé J. Exaggerated auditory startle responses in patients with spinal cord injury. J Neurology 2008: 255: 703-9.
5. Kumru H, Soto O, Casanova J, Valls-Solé J. Motor corte excitability changes during imagery of simple reaction time. Experimenta Brain Research 2008; 189: 373-8.
6. Valls-Solé J, Kumru H, Kofler M. Interaction between startle and voluntary reactions in humans. Exp Brain Res. 2008; 187:497-507
7. Kumru H, Opisso E, Valls-Solé J, Kofler M. The effect of a prepulse stimulus on the EMG rebound following the cutaneous silent period. J Physiology. 2009; 587:587-95.
8. Kumru H, Kofler M, Valls-Solé J, Portell E, Vidal J. Brainstem reflexes are enhanced after severe spinal cord injury and reduced by continuous intrathecal baclofen. Neurorehabilitation neural repair. 2009. In press.

Capitulo 9. - Comentarios i Conclusiones

Las observaciones hechas como resultado de los estudios presentados aquí indican lo siguiente:

1. La preparación para la ejecución de una acción implica el aumento de actividad a nivel subcortical.

La estructura activada por el ESA es una parte importante en el circuito subcortical motor. En los experimentos descritos aquí, el ESA proporcionó la energía requerida por el sistema para ejecutar el programa motor entero antes de que llegue a tener efecto el comando voluntario. En una situación no-experimental, la vía subcortical motora, altamente excitable, requeriría solamente una entrada excitatoria del tracto descendente córtico-reticular para su activación. Al realizar un movimiento balístico voluntariamente, este último paso en el aumento de la excitabilidad de los circuitos motores se genera a nivel cortical y se transmite hacia zonas cortico-subcorticales (figura 7). El aumento en la excitabilidad de la via corticospinal, responsable del aumento en el tamaño del PEM que ocurre 60-100 ms antes del inicio de la actividad del EMG (Pascual-Leone et al. 1992; Davey et al. 1998), serviría como el disparador para el movimiento previsto, preparado convenientemente y guardado para su ejecución, a nivel subcortical.

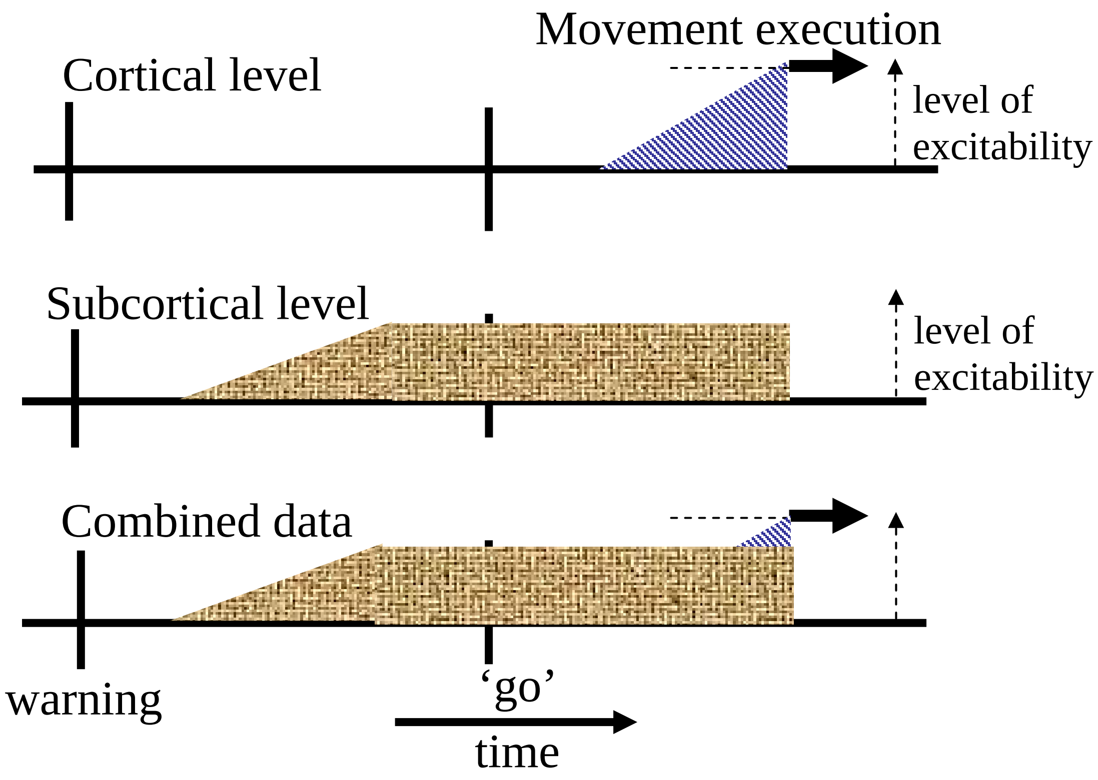


Figura 7. *Al realizar un movimiento balístico voluntariamente, el último paso en el aumento de la excitabilidad de la vía motora se genera a nivel cortical y se transmite hacia tractos córtico-subcorticales. A nivel subcortical, la excitabilidad está ya probablemente aumentada en el momento de la señal imperativa (por ello, la RS es mayor en condiciones de preparación). Sin embargo, el nivel de excitabilidad subcortical no es suficiente para ejecutar el movimiento ya que probablemente existe al mismo tiempo una cierta inhibición de control. En esta situación, cualquier pequeño incremento de energía llevaría a la ejecución del movimiento.*

2. La preparación subcortical motora ocurre no solamente en el tiempo de reacción simple sino que también se observa en tareas de tiempo de reacción de elección. Por ejemplo, en aquellas ocasiones en las que los sujetos se enfrentan con un número limitado de posibilidades e incluso en casos en que existe la posibilidad de no reacción.

En el estudio de la excitabilidad de los circuitos motores subcorticales en casos de Go/noGo y tREF, hemos confirmado que los sujetos voluntarios sanos muestran un cierto grado de preparación antes de la presentación de la señal imperativa y, de esta manera, el estímulo de sobresalto facilita la ejecución del programa motor que ya está preparado. A menudo, esta situación comporta la ejecución de acciones que el sujeto no hubiera querido realizar. Prueba de ello son los errores que tienen lugar en determinadas situaciones de stress en las que el factor tiempo juega un papel importante.

Aunque la preparación implica una mayor posibilidad de errores en el tiempo de reacción de elección, es probable que en condiciones que requieren movimientos de gran velocidad, los sujetos prefieren preparar su sistema motor para la reacción esperada antes que quedarse en reposo incluso antes de conocer con exactitud el tipo exacto de movimiento requerido. Un ejemplo de ello es la reacción del portero ante el penalti (Figura 8).

Figura 8. *Un ejemplo de reacción de elección en el que el sujeto empieza la reacción antes de saber con seguridad la dirección de la pelota.*

3. La reacción de sobresalto y los efectos de un estímulo en el tiempo de reacción son dos efectos diferentes, que responden de manera diferente a la inhibición por prepulso.

Evidencia de dicha disociación entre la reacción de sobresalto y el efecto StartReact se ha observado también en el estudio de la habituación: Mientras que la habituación de la RS es prominente (Brown et al. 1991a; Chokroverty et al. 1992; Kofler et al. 2001), el fenómeno StartReact se observa consistentemente en el curso de una serie de experimentos (Valls-Sole et al., 1997; Valldeoriola et al. 1998). La RS muestra también una disminución de la habituación cuando se induce durante la preparación motora en comparación al reposo.

Ésta puede ser consecuencia del aumento progresivo de la excitabilidad en la vía reticulospinal que tiene lugar durante la preparación del movimiento. Tal aumento de la excitabilidad está preparando los músculos implicados en la ejecución del programa motor, incluyendo los músculos que participan en la reacción y los músculos posturales (Brown et al. 1991b; Valls-Solé et al. 1999a). Una consecuencia conocida del aumento de excitabilidad en la via subcortical motora es el inicio anticipado en una carrera que ocurre aparentemente antes del disparador (figura 9).

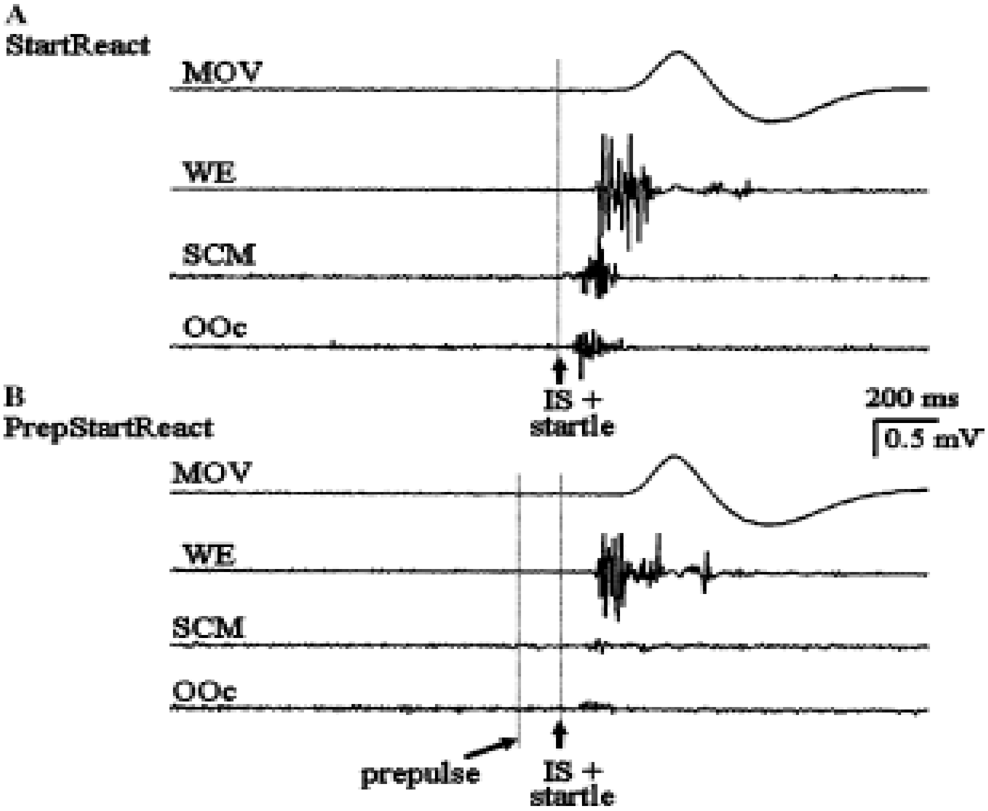


Figura 9. *Experimentos de tiempo de reacción en condiciones StartReact (a) y PrepStartReact (b). Nótese el marcado decremento de la RS en los músculos esternocleidomastoideo y orbicular de los párpados, sin modificación concomitante del efecto de acortamiento del tiempo de reacción en la condición PrepStartReact en comparación a la condición StartReact*.

Los músculos que no participan directamente en la reacción retienen la reactividad al sobresalto y el efecto de prepulso puede expresarse plenamente al no ser incluido en el aumento de excitabilidad típico del programa motor preparatorio. Más estudios sobre la relación entre las acciones voluntarias y reflejas son necesarios para entender completamente el papel de los circuitos motores subcorticales en la organización y ejecución de los actos motores humanos.

4. El ESA induce un acortamiento marcado de la latencia de las sacadas dirigidas a una diana externa, sin que se modifiquen las características intrínsecas del movimiento ocular.

Esto sugiere que las sacadas están programadas principalmente en un nivel donde el ESA puede accionarlas. Esta acción puede utilizar un cortocircuito en el procesamiento sensorial pero esto no parece afectar la exactitud del movimiento al enfocar la diana. La ejecución involuntaria de movimientos sacádicos preparados no permite la modificación voluntaria de la direccionalidad de la mirada pero los resultados del experimento realizado indican que el tiempo requerido para el análisis de las señales incluidas en la diana es el mismo en condición basal y en la condición StartReact. Probablemente, los movimientos sacádicos pueden programarse de antemano si se sabe cuál será la diana. Esto es, por ejemplo, lo qué puede suceder al activar la reacción de escape o de lucha después de reconocer algunas características faciales en el caso de un agresor sospechado (figura 10).

Figura 10. *Expresiones del estado emocional en la cara. Caras enojadas (primera foto) y (en segundo lugar) felices.*

5. La preparación subcortical motora se reduce significativamente durante la ejecución de otro movimiento voluntario.

La ejecución de movimientos oscilatorios rítmicos con una extremidad interfiere en la ejecución de movimientos balísticos con el miembro contralateral. Esto fue observado tanto en ensayos conteniendo un ESA como en aquellos en que no existía ESA. El mismo efecto ha sido observado en las dos condiciones, lo que sugiere que la preparación de las zonas subcorticales motoras fue reducida con respecto a la situación en que el sujeto no estaba efectuando ningún movimiento con la mano contralateral. La preparación insuficiente de los circuitos motores subcorticales puede explicar el retraso en la ejecución del tiempo de reacción cuando se realizan simultáneamente movimientos contralaterales. Las observaciones efectuadas en este trabajo pueden ser de interés para el estudio de la fisiología de la coordinación entre extremidades y podrían contribuir a mejorar nuestra comprensión de los mecanismos subyacentes al fenómeno de interferencia entre tareas. No se sabe si el entrenamiento podría conducir a una situación en la cual este defecto puede ser compensado. Indudablemente, existen personas que pueden activar rítmicamente ambas manos por separado (Figura 11). La posibilidad de explorar la realización de movimientos balísticos mediante el fenómeno StartReact mientras se están realizando movimientos rítmicos contralaterales ayudaría a entender los efectos del aprendizaje y del entrenamiento en la plasticidad de los circuitos motores subcorticales.

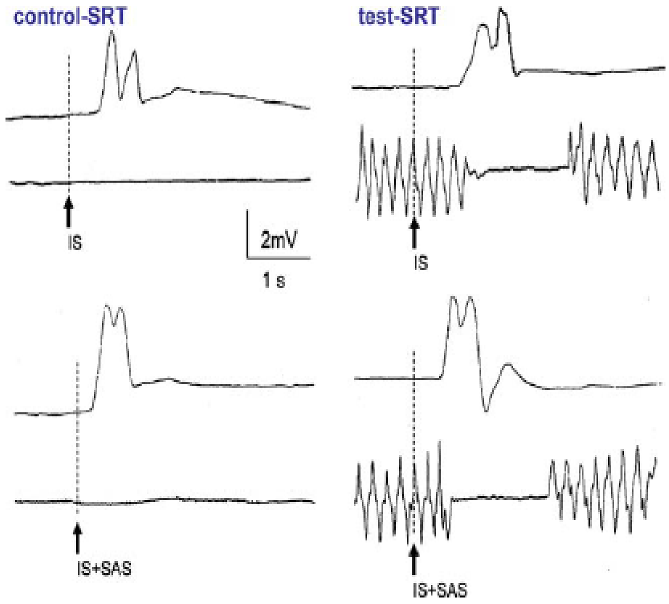


Figura 11. *Registros del efecto de la activación rítmica de una mano cuando se efectúan movimientos oscilatorios con la otra mano, en un sujeto sano representativo. Los trazos superiores muestran el efecto sin la aplicación simultánea de un ESA, mientras que los trazos inferiores muestran los cambios cuando se aplica un ESA. SAS: startling acoustic stimulus*

Capitulo 10.- Contribuciones recientes al avance del conocimiento de la relación entre la reacción sobresalto y el movimiento voluntario. Ideas para líneas futuras de investigación.

10.1. Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2008) Motor preparation in an anticipation-timing task. Exp Brain Res 190: 453-61.

The authors employed a startling stimulus to investigate the temporal course of motor preparation during a stop-signal anticipation-timing task. Participants timed a key release coincident with the sweep of a clock hand reaching a target. On some trials, the clock hand stopped prior to reaching the target (and participants were requested to refrain from responding). Trials were accompanied by either a startling acoustic stimulus (124 dB) or control stimulus (82 dB). Subjects made a similar number of errors (non stopping when the clock hand stopped before the target) in trials with and without SAS. The authors concluded that while some advance preparation of motor circuits was evident, subcortical pre-programming and storage of the motor command in circuits common to the voluntary and startle response pathways was not completed well in advance of response production.

Critical comments: *The control stimulus was a sound that could have also acted as trigger of some reactions. Therefore, the control and test trials could have not been different. The StartReact effect can happen with low intensity stimuli. The level of motor preparation is the most important player in* *the mechanism of StartReact. In Carlsen's et al.'s (2008) experiment, subjects could have had been fully prepared until the clock hand reached the criticial point.*

10.2. Maslovat D, Carlsen AN, Ishimoto R, Chua R, Franks IM (2008) Response preparation changes following practice of an asymmetrical bimanual movement. Exp Brain Res. 190:239-49.

The authors have studied the effects of practice on the advance preparation of an asymmetrical bimanual movement. Startle and non-startle (control) trials from early and late practice were compared on various kinematic and EMG measures. Results indicated that it is possible to pre-program a bimanual asymmetrical movement, and that advance preparation of movement amplitude changes with practice. Evidence was also provided that the different amplitude movements were performed using similar EMG timing between limbs, while adjusting the relative ratio of EMG amplitude. The authors concluded that learning of the task appeared to be related to the ability to prepare the correct asymmetrical EMG amplitudes rather than changing the timing of the EMG pattern.

Critical comments. *This is an evidence for the possibility of plastic changes in subcortical motor circuits related to motor preparation. However, it remains to be tested if a ballistic movement can be performed with one hand without activating simultaneously the other hand. In their manuscript, the authors performed discrete bimanual asymmetric movements and saw* *activation with the same EMG timing. Therefore, subjects had preparation in both sides. A working hypothesis is that it is impossible to refrain from activating the contralateral hand when doing a ballistic unilateral movement in the context of a StartReact effect because of not enough time for inhibition of the unwanted co-activation.*

10.3. Carlsen AN, Chua R, Dakin CJ, Sanderson DJ, Inglis JT, Franks IM (2008b) Startle reveals an absence of advance motor programming in a Go/No-go task. Neurosci Lett. 434: 61-5.

The authors showed that presenting a startling stimulus in a simple reaction time (RT) task can involuntarily trigger the pre-programmed response. However, this effect was not seen when the response was programmed following the imperative stimulus (IS) providing evidence that a startle can only trigger pre-programmed responses. In a "Go/no-Go" (GNG) RT task the response may be programmed in advance of the IS because there exists only a single predetermined response. The authors aimed to examine if startle could elicit a response in a GNG task. Participants completed a wrist extension task in response to a visual stimulus. A startling acoustic stimulus (124dB) was presented in both Go and no-Go trials with Go probability manipulated between groups. The authors found that a startle did not significantly speed RT and led to more response errors. This result is similar to that observed in a startled choice RT task, indicating that in a GNG task participants waited until the IS complete motor programming.

***Critical comments**. The results presented by the authors in this article are in line with those observed by Kumru et al. (2006). However, the authors did not examine forced choice reaction time. There is a conspicuous difference between forced choice reaction time and Go/no-Go tasks in the fact that inhibition has to come into play in Go/no-Go tasks while not in forced choice reaction time. There is reduced possibility for the study of inhibitory components of the motor acts but one of them, the short-interval intracortical inhibition or SICI (Kujirai et al., 1993) is available for study during reaction time. Preliminary results (Soto et al., 2006 abstract) have shown, however, that SICI does not contribute significantly to the control of corticospinal excitability in preparation for a reaction.*

10.4. Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2008c) Differential effects of startle on reaction time for finger and arm movements. J Neurophysiol. 2009; 101:306-14.

In this paper, the authors hypothesis is that, even though the details of the upcoming response could be stored subcortically and are accessible by the startle volley, directly eliciting the correct movement, certain muscles (e.g. intrinsic hand) are heavily dependent on cortico-motoneuronal connections, and could not be directly subject to the subcortical startle volley in the same way as muscles whose innervations include extensive reticular connections. The authors showed that in the arm task, the presence of a startle reaction led to significantly shorter latency of arm movements compared to the effect of the increased stimulus intensity alone. In contrast, for the finger task, no additional decrease in RT due to startle was observed. Taken together these results suggest that only movements that involve muscles more strongly innervated by subcortical pathways are susceptible to response advancement by startle.

Critical comments. *Many movements require postural adjustments for correct performance. Muscles required for postural adjustments are precisely those that are more heavily innervated by the reticulospinal tract. Certainly, discrete finger movements may not require postural adjustments if the arm is sufficiently stable and this may be an exception to the general rule of the StartReact effect.*

Many motor actions may be governed by the amount of preparation that is allowed for subcortical motor circuits. In the subsequent papers, other authors have recently demonstrated the applicability of the StartReact phenomenon to common daily activities supporting the main conclusions of this thesis: that there is an interplay between subcortical motor circuits activation and voluntary commands. Such interplay leads to fine and accurate performance of fast voluntary movements in healthy persons and its abnormal functioning may be a pathophysiological base for disturbances in motor control in many neurological diseases.

10.5. Tresilian JR, Plooy AM (2006) Effects of acoustic startle stimuli on interceptive action. Neuroscience 142:579-594.

In reaction time (RT) tasks, presentation of a startling acoustic stimulus (SAS) together with a visual imperative stimulus can dramatically reduce RT while leaving response execution unchanged. It has been suggested that a prepared motor response program is triggered early by the SAS but is not otherwise affected. Movements aimed at intercepting moving targets are usually considered to be similarly governed by a prepared program. This program is triggered when visual stimulus information about the time to arrival of the moving target reaches a specific criterion. Tresilian and Plooy (2006) investigated whether a SAS could also trigger such a movement. Their results showed that startling probe stimuli at 85 and 115 ms produced early response onsets but not those at 65 or 135 ms. Sub-threshold stimuli at 115 and 135 ms also produced early onsets. Startle probes led to an increased vigor in the response, but sub-threshold probes had no detectable effects. These data can be explained by a simple model in which preparatory, response-related activation builds up in the circuits responsible for generating motor commands in anticipation of the GO command. The authors concluded that if early triggering by the acoustic probes is the mechanism underlying the findings, then the data support the hypothesis that rapid interceptions are governed by a motor program.

10.6. Queralt A, Weerdesteyn V, van Duijnhoven HJ, Castellote JM, Valls-Solé J, Duysens J (2008a) The effects of an auditory startle on obstacle avoidance during walking. J Physiol. 586:4453-63.

The StartReact effect has been recently observed in a step adjustment task requiring fast selection of specific movements in a choice reaction time task. Therefore, Queralt et al. (2008a) hypothesized that inducing a StartReact effect may be beneficial in obstacle avoidance under time pressure, when subjects have to perform fast gait adjustments. The healthy young adults walked on a treadmill and obstacles were released in specific moments of the step cycle. The presentation of a startle increased the probability of using a long step strategy, enlarged stride length modifications and resulted in higher success rates, to avoid the obstacle. The authors also examined the effects of the startle in a condition in which the obstacle was not present in comparison to a condition in which the obstacle was visibly present but it did not fall. In the latter condition, the obstacle avoidance reaction occurred with a similar latency but smaller amplitude as in trials in which the obstacle was actually released. Finally, the authors concluded that the motor programmes used for obstacle avoidance are probably stored at subcortical structures. The release of these motor programmes by a startling auditory stimulus may combine intersensory facilitation and the StartReact effect.

10.7. Queralt A, Valls-Solé J, Castellote JM (2008b) The effects of a startle on the sit-to-stand manoeuvre. Exp Brain Res 185:603-609.

Simple ballistic movements are executed faster in reaction time task paradigms when the imperative signal (IS) is accompanied by a startling auditory stimulus (SAS). Queralt et al (2008b) examined whether this effect also occurs in complex movements such as the sit-to-stand manoeuvre (STS). Reaction time, measured as the time between IS and take-off (TO), was significantly shortened in test trials when SAS was applied at an interval of 0 ms with respect to IS. The onset latency of EMG bursts recorded from tibialis anterior, lumbar paraspinal, quadriceps and biceps femoris muscles reduced proportionally to the shortening of TO. However, these effects were not observed if SAS was delivered 150 ms after IS, when the manoeuvre had already started. The authors concluded that stimuli acting on subcortical motor structures speed-up but do not otherwise interfere with the execution of the motor programs underlying the STS manoeuvre.

10.8. Walsh E, Haggard P (2008) The effects of acoustic startle on sensorimotor attenuation prior to movement. Exp Brain Res 189:279-88.

The authors investigated the effects of the startle acceleration of response on sensory suppression, a phenomenon linked to the voluntary motor command whereby a tactile stimulus is less likely to be perceived on a moving body-part prior to voluntary movement than at rest. Subjects had to detect weak shocks which were delivered to the index finger after a Go signal on some trials. The authors found that detection rates on movement trials were lower than on non-movement trials, consistent with sensory suppression. In addition, a loud acoustic stimulus was presented at the same time as the Go signal on some trials (startle trials). Reaction times were significantly shorter on startle trials than on other trials, replicating previous startle acceleration of reaction time effects attributed to the operation of subcortical pathways. However, no overall difference has been found in premovement sensory suppression effects between baseline and startle movement trials. Rather, startle acceleration of voluntary reactions produced a corresponding acceleration of sensory suppression. The authors concluded that the results provide evidence for a subcortical contribution to sensory suppression and suggest that sensory suppression is a highly general form of motor and sensory interaction.

Referencias

Bisdorff AR, Bronstein AM, Gresty MA (1994) Responses in neck and facial muscles to sudden free fall and a startling auditory stimulus. Electroenceph clin Neurophysiol 93: 409-416.

Blumenthal TD, Gescheider GA (1987) Modification of the acoustic startle reflex by a tactile prepulse: the effects of stimulus onset asynchrony and prepulse intensity. Psychophysiology 24: 320-327.

Blumenthal TD, Cuthbert BN, Filion DL, Hackley S, Lipp OV, Van Boxtel A (2005) Committee report: guidelines for human startle eyeblink electromyographic studies. Psychophysiology 42:1–15

Boelhouwer AJW, Teurlings RJMA, Brunia CHM (1991) The effect of an acoustic warning stimulus upon the electrically elicited blink reflex in humans. Psychophysiology 28: 133-139.

Boulu Ph, Willer JC, Cambier J (1981) Analyse electrophysiologique du réflexe de clignement chez l'homme: interaction des afferences sensitives segmentaires et intersegmentaires, des afferences auditives et visuelles. Rev Neurol 137: 523-533.

Bour LJ, Aramideh M, Ongerboer DE, Visser BW (2000) Neurophysiological aspects of eye and eyelid movements during blinking in humans. J Neurophysiol 83:166–176.

Bradley MM, Moulder B, Lang PJ (2005) When good things go bad: the reflex physiology of defense, Psychol. Sci. 16 468–473.

Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD (1991a) New observations on the normal auditory startle reflex in man. Brain 11: 1891-1902.

Brown P, Day BL, Rothwell JC, Thompson PD, Marsden CD (1991b) The effect of posture on the normal and pathological auditory startle reflex. J Neurol Neurosurg Psychiatry 54:892-897.

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2003) Startle response is dishabituated during a reaction time task. Exp Brain Res 152:510-518.

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004a) Can prepared responses be stored subcortically? Exp Brain Res 159:301-309.

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2004b) Prepared movements are elicited early by startle. J Mot Behav 36:253-264.

Carlsen AN, Dakin CJ, Chua R, Franks IM (2007) Startle produces early response latencies that are distinct from stimulus intensity effects. Exp Brain Res 176:199-205.

Carlsen AN, Chua R, Timothy Inglis J, Sanderson DJ, Franks IM (2008) Motor preparation in an anticipation-timing task. Exp Brain Res 190: 453-61.

Carlsen AN, Chua R, Dakin CJ, Sanderson DJ, Inglis JT, Franks IM (2008b) Startle reveals an absence of advance motor programming in a Go/No-go task. Neurosci Lett. 434: 61-5.

Carlsen AN, Chua R, Inglis JT, Sanderson DJ, Franks IM (2008c) Differential effects of startle on reaction time for finger and arm movements. J Neurophysiol. [Epub ahead of print].

Castellote JM, Kumru H, Queralt A, Valls-Sole J (2007) A startle speeds up the execution of externally guided saccades. Exp Brain Res 177:129-136.

Chabot CC, Taylor DH (1992) Circadian modulation of the rat acoustic startle response. Behav Neurosci 106:846-852.

Chokroverty S, Walczak T, Hening W (1992) Human startle reflex: technique and criteria for abnormal response. Electroenceph clin Neurophysiol 85: 236-242.

Collewijn H, Van Der Steen J, Steinman RM (1985) Human eye movements associated with blinks and prolonged eye closure. J Neurophysiol 54:11–27

Costa J, Valls-Sole J, Valldeoriola F, Pech C, Rumia J (2006) Single subthalamic nucleus deep brain stimuli inhibit the blink reflex in Parkinson's disease patients. Brain 129:1758-1767.

Davis M, Gendelman PM (1977) Plasticity of the acoustic startle response in the acutely decerebrate rat. J Comp Physiol Psychol 91: 549-563.

Davis M, Gendelman DS, Tischler MD, Gendelman PM (1982) A primary acoustic startle circuit: lesion and stimulation studies. J Neurosci 2: 791-805.

Davis M (1996) Differential roles of the amygdala and bed nucleus of the stria terminalis in conditioned fear and startle enhanced by corticotropin-releasing hormone. In Ono T, McNaughton BL, Molotchnikoff S, Rolls, E. T. and Nishijo, H., editors. Perception, Memory and Emotion. Oxford: Elsevier Ltd. 525-548.

Delwaide PJ, Schepens B (1995) Auditory startle (audio-spinal) reaction in normal man: EMG responses and H reflex changes in antagonistic lower limb muscles. Electroenceph clin Neurophysiol 97: 416-423.

Dimberg U (1990) Facial electromyographic reactions and autonomic activity to auditory stimuli. Biol Psychol 31: 137-147.

Eimer M (1998) The lateralized readiness potential as an on-line measure of selective response activation. Behav Res Methods Instrum Comput 30:146-156.

Evinger C, Shaw MD, Peck CK, Manning KA, Baker K (1984) Blinking and associated eye movements in human, guinea pig and rabbits. J Neurophysiol 52:323–329

Fendt M, Koch M (1999) Cholinergic modulation of the acoustic startle response in the caudal pontine reticular nucleus of the rat. Eur J Pharmacol 370:101-107.

Fisher RJ, Sharott A, Kühn AA, Brown P (2004) Effects of combined cortical and acoustic stimuli on muscle activity. Exp Brain Res 157:1-9

Floeter MK, Rothwell JC (1999) Releasing the brakes before pressing the gas pedal. Neurology 53:664-665.

Furubayashi T, Ugawa Y, Terao Y, Hanajima R, Sakai K, Machii K, Mochizuki H, Shiio Y, Uesugi H, Enomoto H, Kanazawa I (2000) The human hand motor area is transiently suppressed by an unexpected acoustic stimulus. Clin Neurophysiol 111: 178-183.

Gautier CH, Cook EW (1997) Relationship between startle and cardiovascular reactivity Psychophysiology 34: 87-96.

Gehricke JG, Ornitz EM, Siddarth P (2002) DiVerentiating between reXex and spontaneous blinks using simultaneous recording of the orbicularis oculi electromyogram and the electro-oculogram in startle research. Int J Psychophysiol 44:261–268

Gielen SC, Schmidt RA, Van den Heuvel PJ (1983) On the nature of intersensory facilitation of reaction time. Percept Psychophys 34:161-168.

Gogan P (1970) The startle and orienting reactions in man. A study of their characteristics and habituation. Brain Research 18: 117-135.

Gokin AP, Karpukhina MV (1985) Reticular structures in the cat brain involved in startle to somatic stimuli of various modalities. Neurophysiology 17: 278-286.

Graham FK (1975) The more or less startling effects of weak prestimulation. Psychophysiology 12:238-248.

Graham SJ, Scaife JC, Langley RW, Bradshaw CM, Szabadi E, Xi L, Crumley T, Calder N, Gottesdiener K, Wagner JA (2005)Effects of lorazepam on fear-potentiated startle responses in man. J Psychopharmacol 19:249-58.

Grillon C, Ameli R, Wood SW, Merikangas K, Davis M (1991) Fear-potentiated startle in humans: effects of anticipatory anxiety on the acoustic blink reflex. Psychophysiology 28: 588-595.

Haggard P, Eimer M (1999) On the relation between brain potentials and the awareness of voluntary movements. Exp Brain Res 126:128-133

Ho KJ, Kileny P, Paccioretti D, McLean DR (1987) Neurologic, audiologic, and electrophysiologic sequelae of bitemporal lobe lesions. Arch Neurol 44, 982-987

Hoffman HS, Fleshler M (1963) Startle reaction: modification by background acoustic stimulation. Science 141: 928-930.

Hoffman HS, Ison JR (1980) Reflex modification in the domain of startle: I. Some empirical findings and their implications for how the nervous system processes sensory input. Psychol Rev 87:175-189.

Holand S, Girard A, Laude D, Meyer-Bisch C, Elghozi JL (1999) Effects of an auditory startle stimulus on blood pressure and heart rate in humans. J Hypertens 17:1893-1897.

Hori A, Yasuhara A, Naito H, Yasuhara M (1986) Blink reflex elicited by auditory stimulation in the rabbit. J Neurol Sci 76, 49-59.

Horn AK, Buttner-Ennever JA, Suzuki Y, Henn V (1995) Histological identiWcation of premotor neurons for horizontal saccades in monkey and man by parvalbumin immunostaining. J Comp Neurol 359:350–363

Inglis WL, Winn P (1995) The pedunculo-pontine tegmental nucleus: where the striatum meets the reticular formation. Prog Neurobiol 47: 1-29.

Ison JR, Hoffman HS (1983) Reflex modification in the domain of startle. II. The anomalous history of a robust and ubiquitous phenomenon. Psychol Bull 94:3-17.

Ison JR, Sanes JN, Foss JA, Pinckney LA (1990) Facilitation and inhibition of the human startle blink reflexes by stimulus anticipation. Behav Neurosci 104: 418-429.

Isa T, Naito K (1995) Activity of neurons in the medial pontomedullary reticular formation during orienting movements in alert head-free cats. J Neurophysiol 74:73–95.

Jenny AB, Saper CB (1987) Organization of the facial nucleus and the corticofacial projection in the monkey: a reconsideration of the upper motor neuron facial palsy. Neurology 37: 930-939.

Koch M, Kungel M, Herbert H (1993) Cholinergic neurons in the pedunculopontine tegmental nucleus are involved in the mediation of prepulse inhibition of the acoustic startle response in the rat. Exp Brain Res 97: 71-82.

Koch M (1999) The neurobiology of startle. Progr Neurobiol 59,107-128.

Kodsi MH, Swerdlow NR (1997) Regulation of prepulse inhibition by ventral pallidal projections. Brain Res Bull 43:219-228.

Kofler M, Muller J, Reggiani L, Valls-Sole J (2001a) Influence of gender on auditory startle responses. Brain Res 921: 206-210.

Kofler M, Muller J, Reggiani L, Valls-Sole J (2001b) Influence of age on auditory startle responses in humans. Neurosci Lett 307:65-68.

Kofler M, Müller J, Rinnerthaler-Weichbold M, Valls-Solé J (2008) Laterality of auditory startle responses in humans. Clin Neurophysiol 119:309-314.

Kuhn AA, Sharott A, Trottenberg T, Kupsch A, Brown P (2004) Motor cortex inhibition induced by acoustic stimulation. Exp Brain Res 158:120-124.

Kumru H, Urra X, Compta Y, Castellote JM, Turbau J, Valls-Sole J (2006) Excitability of subcortical motor circuits in Go/noGo and forced choice reaction time tasks. Neurosci Lett 406:66-70.

Kumru H, Valls-Sole J (2006) Excitability of the pathways mediating the startle reaction before execution of a voluntary movement. Exp Brain Res 169:427-432.

Landis C, Hunt WA (1939) The startle pattern. New York. Farrar, Strauss and Giroux.

Lang PJ, Bradley MM, Cuthbert BN (1990) Emotion, attention and the startle reflex. Psychol Rev 97: 377-395.

Lang PJ, Davis M (2006) Emotion, motivation, and the brain: reflex foundations in animal and human research. Prog Brain Res 156:3-29.

Lee Y, López DE, Meloni EJ, Davis M (1996) A primary acoustic startle pathway: obligatory role of cochlear root neurons and the nucleus reticularis pontis caudalis. J Neurosci 16:3775-3789.

Libet B, Gleason CA, Wright EW, Pearl DK (1983) Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). Brain 106:623-642.

Liegeois-Chauvel C, Morin C, Musolino A, Bancaud J, Chauvel P (1989) Evidence for contribution of the auditory cortex to audiospinal facilitation in man. Brain 112:375-391.

Lingenhohl K, Friauf E (1994) Giant neurons in the rat reticular formation: a sensorimotor interface in the elementary acoustic startle circuit? J Neurosci 14: 1176-1194.

Lipp OV, Kaplan DM, Purkis HM (2006) Reaction time facilitation by acoustic task-irrelevant stimuli is not related to startle. Neurosci Lett 409:124-127.

MacKinnon CD, Bissig D, Chiusano J, Miller E, Rudnick L, Jager C, Zhang Y, Mille ML, Rogers MW (2007) Preparation of anticipatory postural adjustments prior to stepping. J Neurophysiol 97:4368-4379.

Maslovat D, Carlsen AN, Ishimoto R, Chua R, Franks IM (2008)Response preparation changes following practice of an asymmetrical bimanualmovement. Exp Brain Res. 190:239-49.

Matsumoto JY, Caviness JN, McEvoy KM (1994) The acoustic startle reflex in stiff-man syndrome. Neurology 44: 1952-1955.

McManis MH, Bradley MM, Berg WK, Cuthbert BN, Lang PJ (2001) Emotional reactions in children: verbal, physiological, and behavioral responses to affective pictures. Psychophysiology 8: 222-231.

Nickerson RS (1973) Intersensory facilitation of reaction time: energy summation or preparation enhancement? Psychol Rev 80:489-509.

Nijhuis LB, Janssen L, Bloem BR, van Dijk JG, Gielen SC, Borm GF, Overeem S (2007) Choice reaction times for human head rotations are shortened by startling acoustic stimuli, irrespective of stimulus direction. J Physiol 584:97-109.

Soto O, Kumru H, Valls-Sole J. Short-latency intracortical inhibition preceding movement: Different time-course of modulation during simple and choiche reaction time. Edinburgh 2006. XVIIIth International Congress of Clinical Neurophysiology.

Parent A, Hazrati LN (1995) Functional anatomy of the basal ganglia. II. The place of subthalamic nucleus and external pallidum in basal ganglia circuitry. Brain Res Brain Res Rev 20:128-154.

Pascual-Leone A, Valls-Sole J, Wassermann EM, Brasil-Neto J, Cohen LG, Hallett M (1992) Effects of focal transcranial magnetic stimulation on simple reaction time to acoustic, visual and somatosensory stimuli. Brain 115:1045-1059.

Paylor R, Crawley JN (1997) Inbred strain differences in prepulse inhibition of the mouse startle response. Psychopharmacology 132:169-180.

Queralt A, Weerdesteyn V, van Duijnhoven HJ, Castellote JM, Valls-Solé J, Duysens J (2008a) The effects of an auditory startle on obstacle avoidance during walking. J Physiol. 586:4453-63.

Queralt A, Valls-Solé J, Castellote JM (2008b) The effects of a startle on the sit-to-stand manoeuvre. Exp Brain Res 185:603-609.

Rambold H, El Baz I, Helmchen C (2005) EVect of blinks on saccades before smooth-pursuit eye-movement initiation. Ann NY Acad Sci 1039:563–566.

Ransmayr G, Faucheux B, Nowakowski C, Kubis N, Federspiel S, Kaufmann W, Henin D, Hauw JJ, Agid Y, Hirsch EC (2000) Age-related changes of neuronal counts in the human pedunculopontine nucleus. Neurosci Lett 288:195-198.

Reese NB, Garcia-Rill E, Skinner RD (1995) The pedunculopontine nucleus--auditory input, arousal and pathophysiology. Prog Neurobiol 47:105-133.

Reynolds C, Ashby P (1999) Inhibition in the human motor cortex is reduced just before a voluntary contraction. Neurology 53:730-735.

Reynolds RF, Day BL (2007) Fast visuomotor processing made faster by sound. J Physiol 583:1107-1115.

Rossi A, Scarpini C (1992) Gating of trigemino-facial reflex from low-threshold trigeminal and extratrigeminal cutaneous fibres in humans. J Neurol Neurosurg Psychiatry 55: 774-780.

Sanegre MT, Castellote JM, Haggard P, Valls-Sole J (2004) The effects of a startle on awareness of action. Exp Brain Res 155:527-531.

Siegmund GP, Inglis JT, Sanderson DJ (2001) Startle response of human neck muscles sculpted by readiness to perform ballistic head movements. J Physiol 535:289-300.

Starr A, Caramia M, Zarola F, Rossini PM (1988) Enhancement of motor cortical excitability in humans by non-invasive electrical stimulation appears prior to voluntary movement. Electroencephalogr Clin Neurophysiol 70:26-32.

Swerdlow NR, Geyer MA (1993) Prepulse inhibition of acoustic startle in rats after lesions of the pedunculopontine tegmental nucleus. Behavioral Neuroscience 107:104-117.

Swerdlow NR, Paulsen J, Braff DL, Butters N, Geyer MA, Swenson MR (1995) Impaired prepulse inhibition of acoustic and tactile startle response in patients with Huntington's disease. J Neurol Neurosurg Psychiatry 58:192-200.

Swerdlow NR, Braff DL, Geyer MA (2000) Animal models of deficient sensorimotor gating: what we know, what we think we know, and what we hope to know soon. Behav Pharmacol 11:185-204.

Takahashi H, Iwase M, Ishii R, Ohi K, Fukumoto M, Azechi M, Ikezawa K, Kurimoto R, Canuet L, Nakahachi T, Iike N, Tagami S, Morihara T, Okochi M, Tanaka T, Kazui H, Yoshida T, Tanimukai H, Yasuda Y, Kudo T, Hashimoto R, Takeda M (2008) Impaired prepulse inhibition and habituation of acoustic startle response in Japanese patients with schizophrenia. Neurosci Res. 187-94.

Terao Y, Ugawa Y, Suzuki M, Sakai K, Hanajima R, Gemba-Shimizu K, Kanazawa I (1997) Shortening of simple reaction time by peripheral electrical and submotor-threshold magnetic cortical stimulation. Exp Brain Res 115:541-545.

Timmann D, Musso C, Kolb FP, Rijntjes M, Jüptner M, Müller SP, Diener HC, Weiller C (1998) Involvement of the human cerebellum during habituation of the acoustic startle response: a PET study. J Neurol Neurosurg Psychiatry 65:771-773.

Tresilian JR, Plooy AM (2006) Effects of acoustic startle stimuli on interceptive action. Neuroscience 142:579-594.

Turpin G (1986) Effects of stimulus intensity on autonomic responding: The problem of differentiating orienting and defense reflexes. Psychophysiology 23:1-14.

Valls-Solé J, Cammarota A, Alvarez R, Hallett M (1994) Orbicularis oculi responses to stimulation of nerve afferents from upper and lower limbs in normal humans. Brain Res 650: 313-316.

Valls-Solé J, Solé A, Valldeoriola F, Muñoz E, Gonzalez LE, Tolosa ES (1995) Reaction time and acoustic startle in normal human subjects. Neurosci Lett 195, 97-100.

Valls-Solé J, Valldeoriola F, Tolosa E, Nobbe F (1997) Habituation of the auditory startle reaction is reduced during preparation for execution of a motor task in normal human subjects. Brain Research 751: 155-159.

Valls-Solé J, Rothwell JC, Goulart F, Cossu G, Muñoz JE (1999a) Patterned ballistic movements triggered by a startle in healthy humans. J Physiol 516: 931-938.

Valls-Solé J, Valldeoriola F, Molinuevo JL, Cossu G, Nobbe F (1999b) Prepulse modulation of the startle reaction and the blink reflex in normal human subjects. Exp Brain Res 129:49-56.

Valls-Solé J, Veciana M, León L, Valldeoriola F (2002) Effects of a startle on heart rate in patients with multiple system atrophy. Mov Disord 17: 546-549.

Valls-Sole J (2004) Contribution of subcortical motor pathways to the execution of ballistic movements. Suppl Clin Neurophysiol 57:554-562.

Valls-Solé J, Kofler M, Kumru H, Castellote JM, Sanegre MT (2005) Startle-induced reaction time shortening is not modified by prepulse inhibition. Exp Brain Res 165:541-548.

Walker DL, Davis M (1997) Anxiogenic effects of high illumination levels assessed with the acoustic startle response in rats. Biol Psychiatry 42:461-471.

Wilkins DE, Hallett M, Wess MM (1986) Audiogenic startle reflex of man and its relationship to startle syndromes. Brain 109: 561-573.

Wu MF, Suzuki SS, Siegel JM (1988) Anatomical distribution and response patterns of reticular neurons active in relation to acoustic startle. Brain Res 457: 399-406.

Yeomans JS, Frankland PW (1996) The acoustic startle reflex: neurons and connections. Brain Res Rev 21: 301-314.

Zhao Z, Davis M (2004) Fear-potentiated startle in rats is mediated by neurons in the deep layers of the superior colliculus/deep mesencephalic nucleus of the rostral midbrain through the glutamate non-NMDA receptors. J Neurosci 24:10326–10334.