

EFECTO DE LOS FACTORES
CIRCADIANOS EN LA VIGILANCIA
DURANTE LA REALIZACIÓN DE UNA
TAREA DE CONDUCCIÓN

Enrique Molina Martín

Directores:

Ángel Correa Torres

Daniel Sanabria Lucena



Universidad de Granada

2018

Editor: Universidad de Granada. Tesis Doctorales
Autor: Enrique Molina Martín
ISBN: 978-84-1306-050-7
URI: <http://hdl.handle.net/10481/54448>

Publicaciones de la tesis doctoral:

Correa, A., Molina, E., & Sanabria, D. (2014). Effects of chronotype and time of day on the vigilance decrement during simulated driving. *Accident; Analysis and Prevention*, 67C, 113–118. <https://doi.org/10.1016/j.aap.2014.02.020>

Molina, E., Sanabria, D., Jung, T.-P., & Correa, Á. (2017). Electroencephalographic and peripheral temperature dynamics during a prolonged psychomotor vigilance task. *Accident Analysis and Prevention*.
<https://doi.org/10.1016/j.aap.2017.10.014>

Resumen General

Una de las principales causas de los accidentes de tráfico es la fatiga del conductor, que puede producir distracciones y somnolencia, sobre todo en trayectos largos y monótonos. La capacidad de mantener una buena ejecución en la conducción (o en cualquier otra tarea atencional) durante un período de tiempo más o menos largo se denomina vigilancia, y está sujeta a fluctuaciones y a un deterioro continuado con el paso del tiempo, lo que se conoce como el decremento de vigilancia (Mackworth, 1948). Estas fluctuaciones están moduladas por factores como la motivación, el sueño o los ritmos circadianos, los cuáles hacen referencia a la ritmicidad de ciertas funciones humanas, como el ciclo sueño-vigilia, la producción de hormonas y el rendimiento cognitivo (ver, por ejemplo, Goldstein, Hahn, Hasher, Wiprzycka, & Zelazo, 2007).

Es, por tanto, un objetivo importante de la investigación sobre la fatiga, identificar estas fluctuaciones de la atención que llevan a estados de mala ejecución. Una aproximación a este objetivo es monitorizar una serie de variables psicofisiológicas del conductor, como los movimientos oculares, la temperatura o el electroencefalograma (EEG), para ponerlas en relación con su ejecución al volante. Un sistema que sea capaz de identificar estos estados de baja vigilancia y alertar al conductor tendría importantes implicaciones en la seguridad, más aún si el sistema es capaz de predecir estos estados con antelación.

En esta dirección de predecir estados de baja atención se han desarrollado modelos neurofisiológicos que pretenden predecir la ejecución del conductor a partir de medidas de la actividad cerebral (Chin-Teng Lin et al., 2005). Estos modelos suelen ser específicos del sujeto o de la tarea en la que se aplican, y por tanto, no está aún claro hasta qué punto pueden ser extrapolados a distintos sujetos o tareas.

En esta tesis abordamos la problemática de predecir estos estados de bajo rendimiento en la conducción. Para ello, primero se estudió cómo distintos factores afectaban a la ejecución en una tarea de conducción; segundo, se identificaron índices neurofisiológicos del estado atencional en una tarea sencilla de vigilancia; y tercero, se analizó la capacidad predictiva de un modelo simple extrapolado a distintas tareas atencionales.

En el Experimento 1 analizamos el efecto que la hora del día y el cronotipo tienen sobre el decremento de vigilancia en una tarea de conducción y en una tarea simple de tiempo de reacción, la Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985). Dos grupos de cronotipos extremos (i.e., matutinos vs vespertinos) realizaron la tarea en dos horas distintas (8am y 8pm). Estas dos horas representan dos estados cognitivos diferentes para cada grupo, siendo las 8am la hora de mayor rendimiento para el grupo de matutinos, y las 8pm la de mejor rendimiento para el grupo de vespertinos. Además, durante la tarea de conducción se registró el EEG para analizar las dinámicas de potencia en las principales bandas de frecuencia (i.e., theta, alfa y beta). Los resultados de este estudio mostraron una interacción de los factores circadianos (i.e., cronotipo y hora del día) aunque sólo para el cronotipo vespertino, que mostró una peor ejecución por la mañana que por la noche, tanto en la conducción como en la PVT. Sin embargo, este efecto no se vio reflejado en el EEG, que mostró un incremento de potencia generalizado junto con el paso del tiempo para ambos cronotipos.

En el Experimento 2 estudiamos dos variables psicofisiológicas (el EEG y la temperatura de la piel) como predictores de las fluctuaciones de la atención durante una PVT prolongada de 45 minutos, controlando la influencia de factores circadianos por medio de seleccionar sólo sujetos con cronotipo intermedio y realizar todas las sesiones a horas no extremas para ningún cronotipo. El registro del EEG y de la temperatura se realizó de forma continua durante toda la tarea. Analizamos la potencia de las bandas de frecuencia theta, alfa y beta, y tres medidas de temperatura de la piel, la temperatura distal (registrada en la muñeca, sobre los pequeños capilares superficiales), la temperatura proximal (registrada bajo la clavícula izquierda como un estimador de la temperatura central), y el gradiente distal-proximal (DPG), que es la diferencia entre la temperatura distal y la proximal. Posteriormente, estas variables se pusieron en relación con la ejecución en la PVT, medida como el tiempo de reacción.

Los resultados arrojaron evidencia de una clara relación entre una reducción en la velocidad de respuesta y el aumento de la potencia en las bandas de frecuencia theta y alfa, en zonas cerebrales relacionadas con la red atencional. Asimismo, los modelos lineales mostraron que una mejor ejecución en la tarea se relacionaba con

una disminución de la temperatura distal (registrada en las extremidades cerca de pequeños vasos capilares) y del gradiente (que es la diferencia entre la temperatura distal y la temperatura proximal, medida debajo de la clavícula). Estos resultados mostraron que ambos índices (la potencia del EEG y la temperatura de la piel) podrían ser predictores potenciales de la ejecución de un sujeto en la PVT. Sin embargo, mientras que el EEG varía en un rango de milisegundos, la temperatura corporal tiene un ritmo de variación mucho más lento (del orden de minutos), lo que confiere a estos índices distintas capacidades predictivas según la situación.

El objetivo del Experimento 3 era crear un modelo que permitiera predecir la ejecución en una tarea de conducción usando uno de los índices estudiados en el Experimento 2, esto es, los cambios de potencia en las bandas de frecuencia theta y alfa. Además, este modelo debía ser transferible entre tareas. Es decir, el modelo debía construirse con datos de una PVT y ser capaz de predecir la ejecución en la tarea de conducción. Así, el Experimento 3 constaba de dos tareas, una PVT de 20 minutos y una tarea de conducción de 60 minutos, y durante ambas tareas se registró de forma continua el EEG además de los tiempos de reacción.

Para ambas tareas se realizó un análisis de las dinámicas cerebrales similar al que realizamos en el Experimento 2. Este análisis replicó los resultados de aquel experimento para ambas tareas, es decir, encontramos un incremento de la potencia de theta y alfa relacionado con una peor ejecución (i.e., tiempos de reacción más largos). Además, estas dinámicas aparecían en varias zonas cerebrales, incluyendo algunas de las encontradas en el Experimento 2 y relacionadas con la red atencional fronto-parietal y la red por defecto.

Con estos datos ajustamos un modelo individualizado de regresión lineal para la PVT que relacionaba los tiempos de reacción con los cambios de potencia en estas bandas de frecuencia. Después, este modelo se alimentó con los datos de EEG obtenidos durante la tarea de conducción para obtener una estimación de tiempos de reacción, que fueron correlacionados con los tiempos de reacción reales obtenidos durante la tarea de conducción. Los resultados de esta correlación indicaron que el modelo no era completamente transferible entre tareas, aunque no podemos descartarlo completamente ya que sí funcionó para algunos sujetos

(aproximadamente un tercio del total). Una hipótesis de este resultado es que la complejidad del modelo sea un factor clave a la hora de la generalización, y, por lo tanto, un modelo tan sencillo como el nuestro sólo funcione en situaciones donde las fluctuaciones de atención sean muy marcadas y muy poco influenciadas por otros factores no relacionados con la fatiga.

En síntesis, el objetivo último de esta tesis era proponer un modelo predictivo individualizado de la ejecución en una tarea de conducción a partir de una tarea sencilla como la PVT. En el Experimento 2 hemos analizado dos índices psicofisiológicos que permiten predecir los cambios atencionales en una tarea de vigilancia. Posteriormente, en el Experimento 3, hemos usado uno de estos índices para construir un modelo que permitiera transferir la predicción de la ejecución entre dos tareas distintas, la PVT y una tarea de conducción simulada. Asimismo, hemos mostrado por primera vez el importante papel que juegan los ritmos circadianos en la ejecución durante la conducción.

La aproximación planteada en esta tesis se basa en la generalización de un modelo predictivo usando una tarea simple de vigilancia como base para el modelo. Tal modelo permitiría ajustar de forma individualizada y en unos pocos minutos un sistema de prevención de fatiga, no sólo para la conducción, sino para muchas otras tareas diarias que requieren mantener un nivel de alerta continuado. Estas tareas son comunes en muchos trabajos hoy en día, y en estos casos, los lapsos de atención pueden resultar en graves accidentes. Por lo tanto, la investigación en el desarrollo de este modelo tendría un gran impacto en la seguridad.

Driver's fatigue is one of the main causes of road accidents, as it can produce distractions and drowsiness, especially in long and monotonous roads. The ability to maintain a good performance while driving (or in any other task that requires attention) for a long period of time is called vigilance, and it can present fluctuations and a continuous decline with time on task, a phenomenon known as the vigilance decrement (Mackworth, 1948). These fluctuations are modulated by factors like motivation, sleep or circadian rhythmicity, which refers to the periodicity of several human functions, like sleep-wake cycle, hormone production or even cognitive performance (see for example (Goldstein, Hahn, Hasher, Wiprzycka, & Zelazo, 2007)).

Therefore, a main goal in fatigue research is to identify these attentional fluctuations that can lead to poor performance states. One framework to attain this aim is monitoring subject's psychophysiological variables, like the ocular movements, the body temperature or the electroencephalogram (EEG), and use them as indices of subject's performance on the task. A system that, using these variables, could identify subject's low attentional states and alert the driver of an imminent risk, would have important implications on safety, even more if such a system could identify these states in advance.

Within this framework, some neurophysiological models have been developed to predict a driver's performance from records of the brain activity (Chin-Teng Lin et al., 2005). These models are, generally, subject- or task-specific and is not clear to what extent they can be transfer between subjects or tasks.

In this thesis we addressed the topic of predicting low performance states while driving. To do so, we first studied different factors that can modulate performance in a driving task; second, we studied two neurophysiologic indices of attentional state using a simple vigilance task; and third, we tested the predictive accuracy of a simple regression model when transferred between two different attentional tasks.

In Experiment 1, we studied the effect of time of day and chronotype on the vigilance decrement in a simulated driving task and in a simple reaction time task, the Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985). We tested two

extreme chronotype groups (morning-type and evening-type) at two different moments of day (8am vs 8pm). These two times of the day represented an optimum and sub-optimum cognitive state for each chronotype, being the morning-type in its optimum state at 8am, and the evening-type at 8pm. We also recorded the EEG throughout the driving task to analyze the power dynamics in the main frequency bands (i.e., theta, alpha and beta). Results from this study showed an interaction between the circadian factors (i.e., time of day and chronotype), but only for the evening-type group, while morning-type group showed a very stable performance at both moments of the day. This interaction appeared for both, the driving task and the PVT, but it was not reflected in the EEG, which only showed a generalized power increment with time on task for both chronotypes.

In Experiment 2 we analyzed two psychophysiological variables (EEG and skin temperature) as predictors of the attentional fluctuations while a long 45-min PVT, controlling for the effect of circadian factors by choosing only intermediate-type chronotypes and avoiding extreme hours (i.e., early in the morning or late in the evening) to run the experiment. The EEG and temperature were recorded continuously throughout the task. We examined the power dynamics of the theta, alpha and beta frequency bands from the EEG, and three different skin temperature measures, the distal temperature (recorded from the wrist, over the small superficial capillaries), the proximal temperature (recorded under the left clavicle as an estimator of the core body temperature), and the distal-proximal gradient (DPG), which is the difference between the distal and the proximal temperatures, being a more stable measure. Subsequently, these variables (the EEG frequency power and the three temperature recordings) were related to the performance in the PVT, measured as the reaction time.

Results showed evidence of a clear relationship between a slowing-down in the response time and an increment in power in theta and alpha frequency bands, in brain regions related to the attentional network. Likewise, a linear mixed-model showed that a reduction in the distal skin temperature and in the DPG resulted in an increment of the reaction time (i.e., a poorer performance). These results showed that both indices, the EEG frequency power and the skin temperature were

potential predictors of subject's performance in a vigilance task. However, while the EEG worked on a milliseconds scale, the temperature had a much slower time course, on the scale of minutes, which make the former a better choice as predictor for our next experiment.

In the Experiment 3, our main goal was to develop a model to predict performance in a driving task using some of the indices from Experiment 2, that is, the power dynamics from theta and alpha frequency bands. Also, we aimed to transfer this model between tasks, using the data from the PVT to build the model and then using it to predict performance in the driving task. Thus, in Experiment 3, subjects performed a 20-min PVT and a 60-min simulated driving task, while the EEG was recorded throughout the tasks.

The EEG analyses were similar to those used in Experiment 2, and results from the power dynamics replicated those found in Experiment 2. More precisely, the EEG analyses showed an increment of alpha and theta frequency power related to an increment in the reaction time for both tasks, the PVT and the simulated driving. Also, these frequency dynamics were located in the frontal-parietal attentional network and in the default mode network.

The data from the PVT were used to fit an individualized linear regression model, using the EEG frequency power as predictor of the reaction time. Then, this model was feed with the EEG data from the driving task to obtain estimates of the reaction time, which was finally correlated with the actual reaction time from the driving task. This correlation was positive and significant for barely a third of the subjects. It is possible that the complexity of the model was a key factor when transferring it between tasks, and a simple model as ours only works when the attentional fluctuations are not influenced by other factors unrelated to fatigue.

In sum, in this thesis we have proposed an individualized predictive model of performance in a simulated driving task built from a simpler task like the PVT. In Experiment 2 we have shown that EEG and temperature analyses can grasp the attentional state and can predict (even 2 seconds in advance in the case of the EEG) the reaction time in the PVT. Then, in Experiment 3, results showed that it is possible to transfer a simple regression model and make accurate predictions

between tasks, at least for a few subjects. We have likewise shown for the first time that circadian factors play an important role on driving performance, and that this could also be related to subjects' personality. Thus, if personality could affect the performance stability between sessions, then, although circadian factors were controlled in our last experiment, other personality or mood states could have influence the difference in outcomes between tasks. Therefore, a more complex regression model that accounts for variables related to the subject could be the key for the model to work in most of the subjects.

The approach proposed in this thesis is based on the generalization of a predicting model using a simple task. This model would allow anyone to adjust an individualized and instantaneous system for fatigue prevention, not only for driving tasks, but for many other daily tasks that require of a continuous level of alertness. These tasks are common in many jobs and in many cases, an attentional lapse can result in serious accidents, and therefore, research in such a model will have a big impact in safety.

Introducción

Los accidentes de tráfico son un motivo de preocupación importante hoy en día. Se estima que alrededor del 20% de estos accidentes está causado por la fatiga (Dobbie & Australian Transport Safety Bureau., 2002; Fernandes, Hatfield, & Soames Job, 2010; J. A. Horne & Reyner, 1995; MacLean, Davies, & Thiele, 2003), la cual aumenta en trayectos largos y monótonos (S Folkard, 1997). La construcción de autopistas para comunicar ciudades ha convertido esta situación en algo común actualmente, exigiendo un esfuerzo extra al conductor para mantener la atención en trayectos aburridos durante un período mayor de tiempo.

Así, hay un gran esfuerzo en la investigación actual para prevenir estos accidentes, identificando y previendo estados de fatiga y baja atención en los conductores. El objetivo principal de esta tesis ha sido poder contribuir a esta investigación, identificando índices fisiológicos relacionados con las fluctuaciones de atención y evaluando su capacidad predictiva durante la conducción mediante modelos matemáticos.

Atención, vigilancia y fatiga

La atención es un componente básico de nuestro sistema cognitivo y es fundamental para nuestra supervivencia. Fijar la atención en una tarea nos permite optimizar nuestra ejecución y mejorar el procesamiento de la información que llega al cerebro (Mesulam, 1990; Mountcastle, 1978; Parasuraman, 1998). La atención fue dividida por Posner & Petersen (1990) en tres redes atencionales diferenciadas tanto anatómica como funcionalmente: La red de alerta, la red de orientación y la red de detección de señales, que fue posteriormente renombrada como red ejecutiva, ampliando las funciones que tenía asociadas.

La red de orientación se encarga de seleccionar una localización o modalidad sensorial sobre la que priorizar el procesamiento. La red ejecutiva se encarga de la detección de estímulos, la monitorización y la resolución de conflictos. Por último, la red de alerta se encarga de elevar el nivel de activación como preparación para localizar y responder a un estímulo. Esta activación puede mantenerse durante largos periodos de tiempo (alerta tónica) o períodos muy cortos (alerta fásica).

A veces, la tarea que estamos realizando se extiende en el tiempo y necesitamos mantener la atención durante un período más o menos largo. A esta habilidad se le llama atención sostenida o vigilancia (Davies & Parasuraman, 1982; Oken, Salinsky, & Elsas, 2006; Parasuraman, 1998), y es un proceso costoso para nuestro cerebro, lo que implica que aparezcan fluctuaciones de nuestra capacidad atencional (Huang, Jung, & Makeig, 2009), y, eventualmente, un deterioro de esta capacidad que resulta en un fenómeno conocido como el decremento de vigilancia.

El decremento de vigilancia fue descrito por el psicólogo Norman Mackworth (Mackworth, 1948) cuando investigaba por qué los operarios de radar en la Segunda Guerra Mundial no detectaban todas las señales en la pantalla que indicaban la presencia de submarinos enemigos. Mackworth encontró que los fallos de detección de estas señales aparecían en los primeros 15 minutos –o incluso antes si las demandas de la tarea eran elevadas– y seguían aumentando de forma gradual con el paso del tiempo. Es decir, el decremento de vigilancia provoca un deterioro del rendimiento atencional en la tarea

Las causas del decremento de vigilancia son todavía motivo de debate en la investigación, existiendo distintos modelos explicativos que veremos más adelante. Más recientemente también se ha observado que existen fluctuaciones cíclicas, con períodos que pueden variar entre 1 y 10 minutos, en la ejecución en tareas de vigilancia (Aue, Arruda, Kass, & Stanny, 2009; Smith, Valentino, & Arruda, 2003). Estas fluctuaciones, que pueden ocurrir a lo largo de toda la tarea, son el resultado de altibajos en el estado atencional (Huang, Jung, & Makeig, 2009) y, al igual que el efecto de decremento de vigilancia, están estrechamente relacionados con la fatiga (Williamson et al., 2011).

La definición de fatiga ha carecido de consenso en el mundo de la investigación (Phillips, 2015) y términos como fatiga mental o somnolencia se usan a menudo como sinónimos de fatiga. Esto es debido, en parte, al carácter multidimensional del constructo de fatiga, que dificulta su operacionalización a la hora de realizar investigaciones, por lo que muchos investigadores se han visto en la necesidad de centrarse en una dimensión del constructo, lo que ha dificultado su generalización.

Una definición que intenta abarcar todas sus dimensiones es la que propone Phillips (2015):

Fatigue is a suboptimal psychophysiological condition caused by exertion. The degree and dimensional character of the condition depends on the form, dynamics and context of exertion. The context of exertion is described by the value and meaning of performance to the individual; rest and sleep history; circadian effects; psychosocial factors spanning work and home life; individual traits; diet; health, fitness and other individual states; and environmental conditions. The fatigue condition results in changes in strategies or resource use such that original levels of mental processing or physical activity are maintained or reduced. (p. 53).

Así pues, es importante tener en cuenta el carácter multidimensional de la fatiga para entender su efecto sobre la vigilancia, y aunque aún no comprendemos completamente los mecanismos biológicos subyacentes por medio de los cuales la fatiga provoca deterioros en la ejecución, parece que estos mecanismos son diferentes dependiendo de si la fatiga es inducida por somnolencia, ya sea ésta debida a la privación de sueño o a factores circadianos (cronotipo y hora del día), por factores relacionados con la tarea, como su dificultad o la motivación del sujeto, o por la interacción de ambos (Balkin & Wesensten, 2011). Para abarcar esta multidimensionalidad, May & Baldwin (2009) proponen un modelo en el que distinguen entre fatiga activa, fatiga pasiva y fatiga relacionada con el sueño.

Fatiga y sueño

El sueño es seguramente la causa más conocida de la fatiga, y relaciona el decremento en ejecución con la privación de sueño o factores circadianos como el cronotipo o la hora del día. Antes de continuar es importante entender la relación de los factores circadianos con la fatiga y la atención.

Los ritmos circadianos hacen referencia al reloj interno que controla la ritmicidad de muchas funciones biológicas en los seres vivos. Estos ritmos se dan en todas las especies, desde organismos unicelulares hasta organismos complejos como el ser

humano, y son de gran importancia para la supervivencia, ya que marcan cambios periódicos en el entorno y controlan funciones básicas del organismo, como la temperatura corporal, la producción de hormonas o los patrones de sueño-vigilia. En los seres humanos, la estructura que actúa como el reloj interno que regula los ciclos, se encuentra situado en el núcleo supraquiasmático del hipotálamo (Ralph, Foster, Davis, & Menaker, 1990).

Aunque los ritmos circadianos son endógenos, es decir, son controlados internamente con independencia de las condiciones externas al organismo, necesitan, sin embargo, de marcadores externos para mantenerse sincronizados, siendo uno de los más importantes el ciclo luz-oscuridad.

Una de las características más interesantes del comportamiento de los ritmos circadianos son las diferencias individuales que se reflejan en desplazamientos de fase de los ritmos. Estos desfases dan lugar a distintos perfiles circadianos, i.e., cronotipos, que se distribuyen en un continuo, con los cronotipos 'matutino' y 'vespertino' situados en cada uno de los dos extremos. El cronotipo puede ser medido por cuestionarios y se refleja en variables fisiológicas como el ciclo de sueño-vigilia o la temperatura (Adan et al., 2012). El grupo de matutinos incluye gente con una mayor activación en las horas de mañana y su ciclo de sueño-vigilia está desplazado a horas más tempranas. Los vespertinos, por el contrario, prefieren acostarse tarde y están más activos por la noche. Cuanto más extremo sea el desplazamiento de los ciclos, más extremo será, asimismo, el cronotipo.

Las diferencias en cronotipo también afectan a las capacidades cognitivas de los sujetos, de forma que los sujetos matutinos mostrarán un mejor rendimiento por la mañana, mientras que los vespertinos serán mejores por la noche. Esta interacción entre cronotipo y hora del día se conoce como el 'efecto de sincronía' (May & Hasher, 1998).

Volviendo a los estudios sobre la fatiga producida por sueño, estos son predominantes en la literatura sobre fatiga y atención, ya que el protocolo de privación de sueño es una forma sencilla de acentuar el deterioro en la ejecución de las tareas. Por lo tanto, gran parte de los modelos y teorías sobre fatiga y

ejecución derivan de estos estudios (e.g., el modelo de los dos procesos, el modelo de los tres procesos, o la hipótesis de la vulnerabilidad frontal).

El modelo de los dos procesos (Borbély, 1982) se basa en la interacción entre un proceso homeostático (S) y un proceso circadiano (C), que regulan juntos los ciclos de sueño-vigila. El proceso homeostático modula el momento de inicio del sueño (i. e., la presión para el sueño) así como la transición a la vigila. El proceso circadiano, por su parte, refleja cambios cíclicos en la activación modulados por la hora del día. Posteriormente, (Folkard & Akerstedt, 1987) incorporó un tercer proceso a este modelo, la inercia de sueño (W), que representa la somnolencia experimentada justo después de despertarse.

La hipótesis de la vulnerabilidad frontal (J. A. Horne, 1993), así como la perspectiva neuropsicológica basada en el sueño (Babkoff, Zukerman, Fostick, & Ben-Artzi, 2005), similares entre sí, predicen que la falta de sueño afectará de forma especial al córtex prefrontal, lo que se reflejará sobre todo en las funciones cognitivas complejas. Sin embargo, estas predicciones encuentran oposición en la literatura. Por ejemplo, Pilcher, Band, Odle-Dusseau, & Muth (2007) encontraron que, a lo largo de 28 horas de privación de sueño, los sujetos podían mantener una buena ejecución en tareas cognitivamente demandantes, mientras que en tareas de vigilancia que requerían un uso menor de funciones ejecutivas, la ejecución se deterioraba con el tiempo.

Aunque los modelos descritos arriba nos han permitido avanzar en el conocimiento de los efectos más generales de la fatiga en la vigilancia, no nos permiten hacer predicciones precisas de la ejecución ya que no tienen en cuenta variables específicas al sujeto (e.g., motivación) o a la tarea (e.g., tiempo en tarea) que entran en juego al tener en cuenta las otras dimensiones de la fatiga, esto es, la fatiga activa y la fatiga pasiva, y los modelos usados para explicarlas.

Modelos de fatiga

La fatiga activa aparece cuando estamos realizando activamente una tarea y estamos completamente centrados en ella. Esto afecta al rendimiento y produce fluctuaciones de la atención y el decremento de vigilancia, lo que se explica

mediante el modelo de los recursos limitados (Helton & Warm, 2008), que se basa en la hipótesis de que los recursos atencionales disponibles no son infinitos. Así, las tareas que demandan el uso continuado de estos recursos conducen al agotamiento del sistema y la consiguiente aparición de fluctuaciones en la ejecución que se hacen más frecuentes conforme aumenta la duración de la tarea.

Por último, la fatiga pasiva sería lo opuesto a la fatiga activa: La capacidad atencional se resiente debido a la monotonía y la baja demanda de la tarea. En línea con esta explicación tenemos el modelo de la distracción o el aburrimiento. Este modelo propone que el decremento de vigilancia se debe a la falta de incentivos exógenos para mantener la atención, de forma que en los intervalos entre estímulos los participantes pierden interés en la tarea y empiezan a responder de forma automática, mientras se concentran en pensamientos que no tienen que ver con la tarea. Es decir, se produce un cambio atencional hacia la red por defecto del cerebro (Mason et al., 2007). La red por defecto se ha definido como una red activa cuando nuestra atención está más enfocada en estímulos internos que en estímulos externos (Greicius, Krasnow, Reiss, & Menon, 2003a; Weissman, Roberts, Visscher, & Woldorff, 2006). Bajo este modelo, la red se activa cuando el sujeto no está realizando ninguna actividad cognitiva demandante. En el momento en que el sujeto se centra en la tarea, los recursos disponibles se derivan hacia las zonas cerebrales necesarias para realizar la tarea.

La teoría de los recursos limitados y la teoría de la distracción han sido predominantes en los últimos años, pero estudios recientes están mostrando resultados que son difíciles de explicar por ambas teorías. Así, inconsistente con la teoría de los recursos limitados, se ha visto que se puede mejorar la ejecución aumentando la implicación del sujeto en la tarea, incluso si aumentan las demandas de ésta (Smallwood & Schooler, 2006). También se ha visto que aumentando la atención en la tarea (manipulando la valencia de los estímulos) no mejora el rendimiento (Grier et al., 2003), algo que es incompatible con la teoría de la distracción.

Para incluir estos resultados, recientemente se ha propuesto otro modelo, el modelo del control de recursos (Thomson, Besner, & Smilek, 2015). Según esta teoría, los pensamientos autogenerados es el estado natural de los sujetos, por lo

que siempre hay una tendencia a centrar los recursos en la red por defecto. Así, el modelo explica el decremento de vigilancia no como causa de un agotamiento de los recursos, sino como un fallo de la red ejecutiva de mantener los recursos en la tarea, lo que produce que, con el tiempo, cada vez más recursos se destinen a la red por defecto.

Además, este modelo también explica las fluctuaciones de la atención, como un mecanismo de competencia por los recursos entre la tarea y los pensamientos autogenerados, que daría lugar a alternancias en actividad entre las áreas cerebrales relacionadas con la tarea y las relacionadas con la red por defecto.

Bases neurales de la vigilancia

A la hora de estudiar y poner a prueba estos modelos, hay que valorar la gran importancia que han tenido las técnicas de neuroimagen, tales como el electroencefalograma (EEG) o la resonancia magnética funcional (fMRI). Estas técnicas han jugado un papel fundamental para ayudarnos a comprender mejor las áreas implicadas en la vigilancia y los mecanismos biológicos subyacentes. La literatura hace referencia a estructuras subcorticales que forman el sistema reticular ascendente y actúan como moduladores de los ciclos de sueño-vigilia. Estas estructuras incluyen el tálamo, el hipotálamo, el núcleo supraquiasmático y el locus coeruleus (Aston-Jones, 2005; Aston-Jones, Chen, Zhu, & Oshinsky, 2001; Datta & MacLean, 2007; Hastings, Reddy, & Maywood, 2003; Saper, Scammell, & Lu, 2005). El sistema reticular ascendente comprende, asimismo, dos vías principales hacia la corteza cerebral, una vía dorsal a través del tálamo, y una vía ventral a través del área hipotalámica lateral y el preencéfalo basal (Saper et al., 2005; Siegel, 2004), y juntas conforman el sistema subyacente a la red atencional fronto-parietal (Mesulam, 1990; Posner & Petersen, 1990), que incluye el córtex frontal y el córtex cingulado anterior, en la parte anterior de la corteza, y el lóbulo parietal posterior, el colículo superior y el núcleo pulvinar del tálamo en la parte posterior. El sistema anterior está relacionado con funciones ejecutivas, mientras que el sistema posterior lo está de la orientación espacial y la integración multisensorial.

Recientemente también se ha incluido la red por defecto dentro de los sistemas implicados en las fluctuaciones atencionales (Eichele et al., 2008). La red por defecto está formada por una serie de estructuras que están más activas durante periodos de descanso que durante periodos en los que se está realizando alguna tarea experimental (Raichle et al., 2001). La activación de esta red es una parte fundamental para explicar el modelo de los recursos limitados y las estructuras que forman esta red incluyen el cíngulo posterior, el precuneus y el córtex prefrontal medial.

Marcadores fisiológicos de la vigilancia

Nos centraremos en dos índices psicofisiológicos que han sido usados en diversos estudios como marcadores del rendimiento y la fatiga durante tareas de vigilancia: El electroencefalograma (EEG) y la temperatura corporal periférica.

El electroencefalograma

Numerosos estudios han mostrado que es posible predecir cambios en la ejecución del sujeto, y por lo tanto en su estado atencional, monitorizando los cambios producidos en el EEG. El hecho de que el EEG sea una medida directa de la actividad neural y su inmejorable resolución temporal han contribuido a que el EEG se haya convertido en uno de los índices más usados para estudiar los cambios atencionales durante tareas de vigilancia.

El registro del EEG se basa en medir las fluctuaciones de potencial producidas por la actividad sincrónica de grandes grupos de neuronas en distintas zonas del cerebro. Para poder analizar los datos recogidos es necesario primero diferenciar aquellos que están relacionados con el fenómeno que queremos estudiar de los producidos por cualquier otra actividad cerebral sin relación. Para ello, los datos son anclados a un determinado evento y promediados a lo largo de muchos ensayos, de forma que la naturaleza estocástica de la actividad cerebral nos garantizará que los cambios neurales no relacionados con nuestro fenómeno se anularán entre sí, amplificando la relación señal-ruido. Este procedimiento nos

permite analizar los datos en el dominio del tiempo mediante un análisis de potenciales evocados, obteniendo una relación entre los cambios de voltaje y el tiempo. Los potenciales evocados se han usado en varios estudios para estudiar el decremento de vigilancia (Käthner, Wriessnegger, Müller-Putz, Kübler, & Halder, 2014; Martel, Dähne, & Blankertz, 2014; Ramautar, Romeijn, Gómez-Herrero, Piantoni, & Van Someren, 2013).

También es posible realizar un análisis en el dominio de la frecuencia. El análisis de frecuencias asume que existe cierta ritmicidad en la actividad neural, y aplica técnicas como el análisis de Fourier para descomponer espectralmente en distintas bandas de frecuencia los datos recogidos, y estudiar la contribución de cada banda de frecuencia a la actividad relacionada con el fenómeno a estudiar. En general, las frecuencias se agrupan en cinco bandas de frecuencias: Delta (1 – 4 Hz), Theta (4 – 8 Hz), Alfa (8 – 12 Hz), Beta (12 – 30 Hz) y Gamma (más de 30 Hz), cada una de las cuales se asocia con distintos aspectos funcionales.

Alfa es la frecuencia predominante en el cerebro y se ha relacionado con procesos atencionales en numerosos artículos. Sin embargo, también se ha comprobado que los límites de la banda alfa no son estables y varían dependiendo de la persona o de la edad. Es más, alfa puede dividirse a su vez en varias sub-bandas de frecuencia que podrían reflejar distintos procesos cognitivos (ver la revisión de Klimesch, 1999). Esta división se hace a partir del cálculo individualizado de la frecuencia alfa (IAF), que divide la banda de frecuencia en alfa superior (IAF + 2 Hz), y alfa inferior (IAF – 4 Hz), siendo esta última la más relacionada con la alerta fásica. Una vez obtenido el IAF, es posible ajustar igualmente la banda theta, cuyo límite superior coincidiría con IAF – 4 Hz. Este punto se denomina frecuencia de transición (TF) y su cálculo es crucial para evitar que la desincronización de alfa (relacionado con un aumento atencional) se vean enmascarados por la sincronización de theta.

Estos procesos (sincronización y desincronización de theta y alfa) están estrechamente ligados a las fluctuaciones de la atención, de forma que theta y alfa muestran una atenuación de potencia en periodos de concentración o de alto rendimiento cognitivo (Gruber, Klimesch, Sauseng, & Doppelmayr, 2005; Okogbaa, Shell, & Filipusic, 1994). Asimismo, los patrones de sincronización y

desincronización de alfa se han asociado con el potencial P300, relacionado con componentes atencionales (Käthner et al., 2014; Sergeant, Geuze, & van Winsum, 1987; J Yordanova, Kolev, & Polich, 2001).

Delta se encuentra por debajo de la banda theta, y presenta una alta actividad durante el sueño. Por último, un incremento de beta se relaciona con un esfuerzo cognitivo (Craig et al., 2012; Huang et al., 2007) y con el nivel de alerta (Eoh, Chung, & Kim, 2005).

La principal ventaja del análisis de frecuencias sobre el análisis de potenciales evocados es que aquel no necesita estar anclado a un evento discreto ni requiere de un promediado de datos recogidos a lo largo de varios ensayos. Esto permite obtener una medida continua e inmediata del estado atencional del sujeto. Un problema del análisis de frecuencias (y del EEG en general) es que, según el área cerebral donde se originen, las fluctuaciones de frecuencia pueden afectar a distintos procesos mentales. Además, como apuntan Craig et al. (2012), la baja densidad de las redes de electrodos, unida al efecto dispensor del cráneo, dificulta el aislamiento de la señal, así como la localización de la fuente donde se produce dicha señal.

Una solución a este problema es el análisis de componentes independientes (ICA) (Bell & Sejnowski, 1995; Comon, 1994). El ICA es una técnica de análisis de la señal que permite separar fuentes temporalmente independientes de los datos de EEG. Para obtener estos componentes independientes el ICA utiliza la información contenida en los propios datos, asumiendo que distintas actividades neurales deben seguir cursos temporales cuasi-independientes unos de otros. De esta forma, la actividad temporalmente coherente recogida por todos los electrodos se agrupa en un mismo componente. Cada componente incluye además su proyección en cada electrodo, lo que permite obtener la fuente donde ha sido generado.

La temperatura periférica

Uno de los mayores inconvenientes del análisis de EEG como predictor de fatiga es su naturaleza intrusiva. Los estudios de EEG se llevan a cabo con una red de electrodos que deben registrar continuamente la actividad cerebral, y que son

altamente sensibles al movimiento muscular, lo que complica su uso en situaciones reales de conducción. Además, los datos recogidos deben ser procesados para su interpretación, lo cual implica incluir en la situación real de conducción, el hardware necesario para el procesamiento. Un marcador fisiológico que podría solventar estos problemas es la temperatura corporal.

La relación entre temperatura y vigilancia se conoce desde hace tiempo. Así, Kleitman, Titelbaum, & Feiveson (1938) propuso que la temperatura corporal era un mecanismo regulador del rendimiento. Este mecanismo se ha explicado mediante una alteración de la función sináptica causada por cambios en la temperatura del cerebro (Kenneth P Wright, Hull, & Czeisler, 2002), de forma que una temperatura cerebral más elevada resulta en una transmisión más rápida.

Otros estudios han vinculado las fluctuaciones de la temperatura de la piel con la vigilancia. Estos estudios suelen usar tres medidas de temperatura de la piel: La temperatura distal (medida en las extremidades, cerca de pequeños capilares), temperatura proximal (medida alrededor del torso) y el gradiente distal-proximal, que es la diferencia entre la temperatura distal y la proximal. Estos estudios han manipulado la temperatura de la piel mostrando que un incremento de la temperatura proximal corporal resultaba en una mejora del rendimiento en tareas de vigilancia (Raymann & Van Someren, 2007). Igualmente, un incremento del gradiente ha resultado en un aumento de los lapsos y del tiempo de reacción (Tania Lara, Molina, Madrid, & Correa, 2018).

Herramientas para el estudio de la vigilancia

El paradigma típico para estudiar la vigilancia consiste en tareas donde el objetivo es detectar estímulos infrecuentes o inesperados y responder ante ellos. En algunas ocasiones, la tarea del sujeto consiste en responder a todos los estímulos, mientras que, en otras ocasiones, el sujeto debe discriminar ante estímulos 'go' y 'no-go', siendo uno de ellos (generalmente el 'no-go') mucho más frecuente que el otro. En estas tareas las medidas comportamentales típicas para operacionalizar la vigilancia son el tiempo de reacción y las omisiones de respuesta o lapsos. La precisión es otra medida comportamental que se usa en otras tareas 'go/no-go'

donde la relación entre estos estímulos se invierte, es decir, la frecuencia del 'go' es mucho mayor que la del 'no-go', y los sujetos deben inhibir la respuesta ante estos estímulos infrecuentes.

Psychomotor Vigilance Task

Una de las tareas más usadas para evaluar la vigilancia es la Psychomotor Vigilance Task (PVT; Dinges & Powell, 1985). La PVT entra dentro del primer grupo de tareas, es decir, requiere responder a todos los estímulos, los cuáles se presentan de forma inesperada uno tras otro, en un intervalo que va de 2 a 10 segundos. De la PVT se suelen obtener dos medidas de ejecución: El tiempo de reacción y los lapsos, que se definen como tiempos de reacción mayores de 500 ms (Dinges et al., 1997). La PVT es una tarea fácil de implementar y muy versátil, lo que ha dado lugar a un número de variantes, tanto en la presentación y tipo de los estímulos (por ejemplo, auditivos frente a visuales) como en la duración de la tarea. Dado que la PVT fue diseñada para ser sensible al proceso homeostático que nos impulsa a dormir, se ha usado extensamente en estudios de privación de sueño (Dorrian, Rogers, & Dinges, 2005; Lim & Dinges, 2008), y también en la investigación de los ritmos circadianos. Por ejemplo, cronotipo, hora del día y temperatura.

La alta frecuencia de presentación de estímulos y la posibilidad de ajustar su duración ha contribuido a que la PVT sea una de las tareas más usadas para estudiar la vigilancia, y diversos estudios han comprobado la sensibilidad de la PVT ante diversos factores como el efecto de la luz o la cafeína, mostrando que la luz brillante (Figueiro, Bierman, Plitnick, & Rea, 2009; Phipps-Nelson, Redman, Dijk, & Rajaratnam, 2003; Phipps-Nelson, Redman, Schlangen, & Rajaratnam, 2009) o la cafeína (Retey et al., 2006), mejoran el tiempo de reacción en esta tarea en situaciones de privación parcial de sueño.

Varios estudios que usaban la PVT como medida comportamental también han reportado análisis del EEG (Caldwell, Prazinko, & Caldwell, 2003; Chua et al., 2012b), sin embargo, o bien no recogían simultáneamente el EEG y la PVT, o bien no establecían relaciones entre las dinámicas del EEG y la ejecución de la PVT para comprobar los correlatos electrofisiológicos de los tiempos de reacción rápidos y

lentos. En otros estudios, sí ha habido un registro de EEG durante la realización de la PVT. Así, Hoedlmoser et al. (2011) recogieron datos simultáneos de la PVT y de EEG repetidas veces en sesiones de varias horas de duración, lo que permitía comparar la potencia del espectro de EEG con una ejecución global de la PVT durante distintos estados de somnolencia del sujeto. Estos estudios han mostrado un aumento de potencia en las bandas de frecuencia delta y theta, así como una atenuación del potencial P1, cuando la ejecución global de la PVT era peor (i.e., mayor tiempo medio de reacción o mayor número de lapsos). En el segundo estudio de esta tesis, abordamos esta limitación de la literatura, analizando la dinámica de las fluctuaciones de frecuencia del EEG durante la realización de una PVT, además de las áreas cerebrales donde se producían estas fluctuaciones.

Otro de los aspectos menos estudiados de la PVT son sus bases neurales, con apenas un par de estudios donde se identifican. Drummond et al. (2005), mediante el uso de resonancia magnética funcional, identificaron regiones relacionadas con la ejecución en sujetos con y sin privación de sueño. Durante los ensayos con buena ejecución (i.e., menor tiempo de reacción), encontraron un incremento de activación en el giro frontal medial y el lóbulo parietal inferior, es decir, mayor activación en la red atencional fronto-parietal, mientras que, en los ensayos con peor ejecución, la activación se produjo en el giro cingulado, un área incluida en la red por defecto. Estas regiones coinciden con las encontradas en otros estudios sobre vigilancia (Zhu et al., 2018).

En definitiva, la PVT ha demostrado en numerosos estudios su utilidad para captar diferencias en el estado atencional. Sin embargo, sus correlatos neurales, tanto en relación a sus bases neurales como a su efecto sobre análisis de frecuencias del EEG han sido escasos. El segundo estudio de esta tesis abunda en el análisis de estos correlatos, cuya mejor comprensión es necesaria para el tercer objetivo de esta tesis, es decir, su uso como predictor de fluctuaciones de la atención en una tarea de conducción simulada.

Tareas de conducción

Otra tarea cada vez más usada para estudiar las fluctuaciones de la atención son los simuladores de conducción. El hecho de ser una tarea mucho más ecológica y su gran aplicación práctica, están convirtiendo a la conducción simulada en una tarea cada vez más usada en la literatura sobre vigilancia.

Los simuladores de conducción pueden ser tan sencillos como un volante y unos pedales, o tan complejos como el habitáculo real de un coche accionado mecánicamente para simular las fuerzas ejercidas sobre el coche por la propia simulación. Los estudios en situaciones de conducción real son escasos por razones obvias, sin embargo, al comparar la ejecución en simuladores con la conducción real, se ha visto que la variación relativa entre condiciones es similar en ambos tipos de conducción (Hallvig et al., 2013).

En estas tareas, el sujeto debe conducir como si estuviera en una situación real de tráfico (i.e., una autopista), y reaccionar ante determinados eventos, como un frenazo repentino del vehículo que va delante, o un golpe de viento que desvía la trayectoria del coche. La ejecución se mide usando variables como la desviación estándar de la posición lateral, el movimiento del volante, o el control de la velocidad (Kang, 2013), que permiten obtener una medida continua de la ejecución. Sin embargo, también se han usado tareas de conducción que se ajustan a los paradigmas clásicos para estudiar vigilancia. Por ejemplo, Lin et al. (2010) utilizaron una tarea de conducción simulada en la que el sujeto debe responder ante eventos inesperados que desvían el coche. En esta tarea, la ejecución se mide mediante el tiempo de reacción entre este evento y el accionamiento del volante realizada por el sujeto.

La literatura sobre conducción y fatiga ha estudiado el impacto de variables demográficas sobre el riesgo de accidentes, como el sexo o la edad (Di Milia et al., 2011). También se ha analizado el impacto de la privación de sueño o la duración de la conducción. Un factor que ha mostrado tener una clara influencia en el rendimiento de la conducción es el ritmo circadiano. Sin embargo, muchos estudios de conducción ignoran el cronotipo y su interacción con la hora del día como fuente de variabilidad intersujeto, controlándolo en el mejor de los casos, pero no manipulándolo. Así, con nuestro primer estudio pretendimos analizar por

primera vez la interacción entre cronotipo y hora del día en una tarea de conducción.

Marcadores fisiológicos durante la conducción

Además de estudiar factores que influyen en el riesgo de accidentes, otros estudios han puesto en relación la ejecución del sujeto con diversos marcadores fisiológicos con la intención de encontrar índices que permitan monitorizar y predecir fallos atencionales en los conductores, como por ejemplo los movimientos oculares, la respiración, la frecuencia cardíaca, la posición de la cabeza, el número de bostezos o la fuerza de agarre del volante (Kang, 2013).

El análisis de frecuencias del EEG es usado también en numerosos estudios como indicador de fatiga en la conducción, midiendo los cambios en amplitud en las principales bandas de frecuencia (theta, alfa y beta) o combinaciones lineales de ellas (i.e., alfa/beta, theta+alfa/beta). Varias revisiones (Craig et al., 2012; C.-T. Lin et al., 2012; Oken et al., 2006) han recopilado más de 60 artículos en los que se estudia la relación entre los cambios en las principales bandas de frecuencia y la ejecución en tareas de conducción. Estos estudios muestran que el ritmo theta parece ser el indicador más consistente del EEG. Así, un aumento de la somnolencia del sujeto y un deterioro de su ejecución en tareas de vigilancia resultan en un incremento de actividad en esta banda de frecuencia. La potencia de alfa también está directamente relacionada con un decremento en la ejecución, sin embargo, los resultados son más variables y en algunos estudios un incremento de alfa acompaña a una mejora de la concentración y la ejecución. Por último, incrementos en la potencia de beta se relacionan con un incremento en el nivel de alerta, aunque otros estudios han encontrado una relación inversa o incluso ninguna relación en absoluto (Clayton, Yeung, & Cohen Kadosh, 2015; Craig et al., 2012).

En nuestro primer y tercer estudio encontramos un incremento de potencia en las bandas theta y alfa en regiones posteriores y centrales a medida que se deteriora la ejecución en la tarea. Estos datos son muy valiosos a la hora de realizar predicciones en la ejecución de la conducción, aunque estos modelos de predicción

rara vez se han aplicado entre diferentes tareas. Obtener un modelo predictivo de la conducción usando datos de la conducción es algo muy útil, sin embargo, desde un punto de vista práctico, es preferible poder obtener este mismo modelo predictivo con datos de una tarea más sencilla, como la PVT. Es más, la completa generalización del modelo a cualquier tarea donde mantener un nivel elevado de vigilancia es importante, sería el objetivo deseable de nuestra investigación.

Modelos predictivos

Uno de los retos fundamentales en la investigación en vigilancia es obtener sistemas para detectar y clasificar diferentes estados atencionales, y poder de esta forma predecir fallos en la ejecución. Estos sistemas se basan en distintos índices comportamentales y fisiológicos, como el número de parpadeos, la expresión facial, o el ECG.

Estas técnicas han sido extensamente aplicadas en la conducción, con el fin de monitorizar el estado atencional del conductor. Para ello se han desarrollado métodos pretenden obtener una estimación del estado atencional general del sujeto mediante medidas subjetivas de somnolencia (Ting, Hwang, Doong, & Jeng, 2008b) o medidas comportamentales obtenidas mediante alguna tarea que mida vigilancia (Baulk, Biggs, Reid, van den Heuvel, & Dawson, 2008). Sin embargo, estos métodos no permiten modificar esta estimación a lo largo de la tarea y por lo tanto no pueden funcionar en tiempo real. Una de las características más importantes que deben tener los sistemas de predicción es que sean capaces de predecir cambios atencionales durante la tarea de conducción (o cualquier otra que se esté realizando). Así, aunque el estado atencional inicial del sujeto sea óptimo, cuanto más se prolongue la tarea en el tiempo, más probabilidad de producirse un decremento de vigilancia y fluctuaciones de la atención que pueden afectar a la ejecución. Estos sistemas de predicción en tiempo real se pueden clasificar en dos: aquellos que registran comportamientos del conductor, como la posición de la cabeza, y aquellos basados en marcadores biométricos, como la temperatura o el EEG.

En la revisión de Kang (2013) se describen muchos de estos métodos. Dentro del primer grupo, uno de los más usados es el llamado PERCLOS. Este método se basa en monitorizar el tiempo que los parpados cubren más de un 80% del ojo, y dar una alerta cuando este tiempo excede un umbral determinado. Para obtener este indicador, debemos ser capaces de detectar las características visuales del ojo en cualquier condición de luz (de día y de noche), y también a pesar de que el sujeto pueda llevar gafas. Además, uno de sus grandes inconvenientes es que un conductor puede dormirse sin haber empezado a cerrar los ojos. Otros indicadores visuales de la somnolencia del sujeto que se pueden capturar mediante cámaras es la frecuencia de bostezos y la posición de la cabeza, lo que incluye detectar los pequeños cabezazos que se dan al empezar a dormirse.

Un gran problema de esos métodos de predicción es que están enfocados a detectar sólo la fatiga por somnolencia, pasando por alto así los lapsos atencionales causados por la fatiga activa o pasiva. Algunos indicadores biométricos, por el contrario, son útiles como indicadores de somnolencia y también como indicadores de distracción. Entre ellos se encuentran indicadores tales como la frecuencia cardíaca, la temperatura o el electroencefalograma. Sin embargo, estos métodos requieren registrar, filtrar, limpiar y procesar la señal en tiempo real y de forma automática.

Dentro del segundo grupo, el análisis de frecuencias del EEG es, como hemos visto, uno de los índices más fiables para detectar fluctuaciones de la atención, y también uno de los más usados para crear modelos predictivos de tales fluctuaciones. Estos modelos se basan en emparejar características del EEG con alguna medida de ejecución en la tarea de vigilancia, como el tiempo de reacción, para clasificar los ensayos entre buena y mala ejecución, obteniendo así un índice fisiológico del estado atencional. A continuación, estas características del EEG se usan para entrenar el clasificador, que puede ser tan sencillo como una regresión lineal (Chin-Teng Lin et al., 2005), y tan complejo como una red neuronal artificial difusa (F.-C. Lin, Ko, Chuang, Su, & Lin, 2012). En general, los modelos más precisos también son los más complejos, y, por lo tanto, los menos generalizables y los más difíciles de implementar para la detección de la fatiga.

La precisión de estos modelos es bastante alta. Por ejemplo, usando redes neurales entrenadas con características no lineales del EEG, Mardi, Ashtiani, & Mikaili (2011) consiguió una precisión del 83,3% en la clasificación. Con modelos más complejos, usando máquinas de soporte vector (SVM) o redes neuronales difusas, se ha conseguido una precisión del 97%, aunque estos modelos requieren de un conjunto grande de datos (Arjunan, Kumar, & Tzyy-Ping Jung, 2009).

A la hora de buscar marcadores fisiológicos de las fluctuaciones de la atención que puedan incorporarse a modelos predictivos, necesitamos responder a preguntas tales como hasta qué punto estos marcadores son universales, es decir, hasta qué punto son transferibles entre distintas personas y entre distintas tareas. Así, a pesar de que la tendencia es crear modelos basados en características universales, para conseguir una mayor precisión éstos se ajustan individualmente para cada sujeto. La alternativa es usar datos procedentes de una gran muestra para desarrollar modelos que no requieran de estos ajustes individualizados (Stikic et al., 2011), aunque esta aproximación es mucho más costosa.

Por otro lado, la mayoría de los modelos encontrados en la literatura son específicos de una tarea (i.e., se usa la misma tarea para obtener los datos para entrenar el modelo y los datos con los que se pone a prueba), aunque existen unos pocos intentos de transferir los modelos entre tareas. Por ejemplo, Touryan et al. (2014), aplicaron el mismo modelo de regresión lineal a dos tareas, una tarea de conducción y una tarea simple de discriminación visual (RSVP), usando la potencia de la frecuencia del EEG como predictor en ambas tareas. Aunque el modelo debía ser adaptado individualmente a cada sujeto, los resultados mostraron que, para algunos sujetos (7 de 25), era posible transferir el modelo entre tareas y hacer predicciones de la ejecución en cualquiera de estas dos tareas usando los datos recogidos en la otra. Otros estudios han utilizado un paradigma similar para crear un modelo de regresión lineal que pudiera ser transferido entre tareas, aunque solamente en una dirección, esto es, usar la tarea más compleja, por ejemplo, una tarea de conducción, para predecir fluctuaciones de la atención en una tarea simple, por ejemplo, RSVP (Chin-Teng Lin et al., 2005). Esta aproximación implica que los datos para entrenar el modelo han de ser recogidos en el laboratorio, usando configuraciones experimentales complejas y extensas en el tiempo.

Sin embargo, para obtener modelos individualizados de ejecución que puedan ser aplicables en situaciones reales, deberíamos partir de tareas sencillas para crear estos modelos; tareas que puedan ser realizadas en pocos minutos en cualquier lugar, y a partir de las cuales obtengamos modelos sencillos que puedan aplicarse a tareas complejas, es decir, a la situación de riesgo real, ya sea la conducción o el control de tráfico aéreo. Este es uno de los objetivos que perseguimos a lo largo de esta tesis.

Planteamientos de la investigación y objetivos

La motivación de esta tesis se enmarca dentro de dos contextos: Uno teórico y otro más práctico o aplicado, y con tres objetivos principales: Primero, obtener una mejor comprensión de las variables implicadas en las fluctuaciones de la atención, tanto aquellas que pueden influir en estas fluctuaciones, como aquellas en las que se ven reflejadas; segundo, obtener índices confiables que predigan tales fluctuaciones; y, por último, obtener modelos a partir de tales índices que puedan aplicarse a distintas tareas cotidianas. Cada uno de estos tres objetivos fue abordado mediante un determinado estudio, que representan respectivamente cada uno de los tres capítulos de esta tesis. En estos estudios, además, se eligieron tareas en consonancia con estos objetivos: Por un lado, una tarea de tiempo de reacción sencilla y muy validada como marcador de las fluctuaciones de la atención, como es la Psychomotor Vigilance Task o PVT; y, por otro lado, un simulador de conducción, que representa una actividad realizada por la mayor parte de la población adulta y con un alto índice de accidentalidad, siendo además un alto porcentaje de estos accidentes debidos a lapsus de atención.

Estudio 1. Efecto del cronotipo y la hora del día en el decremento de vigilancia durante la conducción simulada.

El objetivo principal de este primer estudio fue tener una visión más amplia de los factores que afectan a la vigilancia y cómo los posibles efectos se ven reflejados en distintas medidas fisiológicas. Para ello decidimos profundizar en el efecto que la hora del día y el cronotipo tienen sobre el decremento de vigilancia, ya que el cronotipo no se había considerado en investigaciones previas. Para realizar este estudio, utilizamos una tarea de conducción simulada por ser muy sensible a las fluctuaciones de la atención, y al mismo tiempo, es realizada por un enorme porcentaje de la población. Durante esta tarea, además de los datos comportamentales con los que obtener un índice de ejecución en la tarea, se registró el EEG para analizar la evolución de potencia en tres bandas espectrales: Theta (4 – 8 Hz), alpha (8 – 12 Hz) y beta (12 – 20 Hz).

Por otro lado, los participantes también realizaron una PVT de 10 minutos previa a la tarea de conducción. La realización de esta PVT era importante para obtener un

índice adicional y confiable del estado atencional de los participantes. Otro índice medido pre y post sesión experimental fueron las medidas subjetivas de activación y estado emocional, que han sido así mismo relacionadas con estados de somnolencia y fluctuaciones de atención. Finalmente, hicimos un registro de la temperatura corporal al inicio de la sesión experimental, con idea de obtener un índice fisiológico del cronotipo de los participantes, que ya había sido previamente evaluado mediante un cuestionario.

El objetivo de este primer estudio era, pues, evidenciar la relación entre variables como el cronotipo y la hora del día y las fluctuaciones atencionales en la tarea, y, al mismo tiempo, identificar variables fisiológicas que pudieran funcionar como índices de tales fluctuaciones.

Los resultados de este estudio confirmaron que el simulador de conducción es una tarea apropiada para medir el decremento de vigilancia y las fluctuaciones atencionales asociadas, y que además es sensible al cronotipo y a la hora del día, igual que la PVT. Sin embargo, el efecto debido a los factores cronobiológicos no se vio reflejado en el EEG, que sólo mostró un efecto debido al paso del tiempo. Por último, tampoco encontramos diferencias debidas al cronotipo en la temperatura corporal, en contra de los que esperábamos.

Estudio 2. Evolución del electroencefalograma y la temperatura periférica durante la tarea PVT.

Los resultados obtenidos en el estudio previo dejaron patente la necesidad de simplificar y explorar más en profundidad el efecto de las fluctuaciones de la atención en la temperatura y el EEG, variables que, aunque han sido muy estudiadas en la literatura, no nos dieron los resultados esperados. Por lo tanto, en este segundo estudio queríamos centrarnos en ver la relación de estas variables con tales fluctuaciones. O, dicho de otra forma, queríamos comprobar si un cambio en el estado atencional del sujeto se reflejaba de forma unívoca en la respuesta de temperatura o de EEG del sujeto.

Para ello, en este segundo estudio simplificamos la tarea usando únicamente una PVT de 45 minutos. También controlamos una serie de variables como el cronotipo

y la hora del día (usando solamente cronotipos intermedios y evitando horas extremas para pasar la tarea), además de otros factores cronobiológicos como las horas de sueño o la ingesta de estimulantes como el café.

El EEG y la temperatura periférica se registraron durante toda la tarea para obtener una medida continua de ambos índices que pudiéramos poner en relación con nuestra medida de rendimiento, en este caso, el tiempo de reacción en la PVT. En este estudio se aplicó el análisis de componentes independientes (ICA) y la localización de dipolos al EEG. La aplicación de ICA nos permite descomponer la señal de los canales en distintos componentes con fuentes y cursos temporales independientes, maximizando así la especificidad de estos componentes con relación a un determinado proceso mental. Por otro lado, la relación de la temperatura con el RT se evaluó mediante tres modelos lineales generalizados (GLM), uno para la temperatura distal (medida en la muñeca), otro para la temperatura proximal (medida en el pecho) y, por último, otro para el gradiente distal-proximal o DPG (la diferencia entre la distal y la proximal).

Los resultados arrojaron evidencia de una clara relación entre una reducción en la velocidad de respuesta y el aumento de la potencia de alpha y theta en zonas cerebrales relacionadas con la red atencional. Asimismo, los modelos lineales mostraron que una mejor ejecución en la tarea se relacionaba con un aumento en la temperatura proximal y con una disminución de temperatura distal y del gradiente. Sin embargo, a diferencia del EEG, la temperatura tenía el inconveniente de su baja resolución temporal, por lo que decidimos descartarlo para nuestra siguiente investigación.

Estudio 3. Evaluación de la transferencia de información basada en EEG entre dos tareas de vigilancia.

El estudio previo mostró que la potencia del EEG, sobre todo en las bandas de alpha y theta, era un buen indicador del rendimiento en la PVT, y, por lo tanto, tenía potencialidad como indicador para otras tareas de atención sostenida. Ahora nos interesaba comprobar si esos resultados eran extrapolables entre tareas diferentes.

Así, el último estudio fue diseñado con la intención de obtener un modelo del estado atencional de una persona que pueda predecir su ejecución en una tarea posterior. La obtención de este modelo supondría un gran avance práctico en la investigación sobre vigilancia y fluctuaciones atencionales, ya que permitiría, a partir de una tarea sencilla, obtener un índice instantáneo del estado atencional de una persona antes de realizar una tarea más compleja y que pudiera suponer un riesgo importante.

A pesar de que modelos similares se han evaluado en la literatura con resultados que invitan al optimismo, uno de los grandes desafíos en el campo es comprender hasta qué punto estos modelos son transferibles entre distintos sujetos y distintas tareas. En el primer caso, los modelos específicos de cada sujeto obtienen significativamente mejores resultados que aquellos basados en grandes muestras de sujetos. Con respecto a la especificidad de tarea, la mayoría de los estudios crean modelos de predicción usando la misma tarea, y aún sabemos poco sobre qué aspectos de tales modelos son transferibles a otras tareas.

En este tercer estudio queremos explorar esta cuestión, evaluando hasta qué punto un modelo obtenido en una tarea corta de atención puede ser transferido a otra tarea diferente. Más concretamente, el objetivo era usar la dinámica espectral del EEG registrado durante una PVT de 20 minutos para obtener un modelo que pudiera predecir fluctuaciones de atención en una tarea de conducción de 60 minutos.

De nuevo aplicamos ICA para el análisis de EEG. Los resultados tanto de la PVT como de la tarea de conducción replicaron los del estudio previo; esto es, obtuvimos componentes con dinámicas y localizaciones similares. Posteriormente, usando GLM obtuvimos un modelo predictivo del RT en la PVT a partir de la potencia en alfa, theta y beta, que fue posteriormente aplicado a los datos registrados durante la tarea de conducción.

Los resultados obtenidos invitan al optimismo, ya que, si bien el modelo no funcionó para todos los sujetos, en los sujetos que sí funcionó la predicción fue bastante precisa.

Estudio I

**Effects of chronotype and time of day
on the vigilance decrement during simulated driving**

1. Introduction

Performance in vigilant attention tasks after 18 hours of extended wakefulness declines until levels equivalent to those produced by the ingestion of the legal maximum amount of alcohol (0.05% blood alcohol concentration) allowed for driving in many countries (Dawson & Reid, 1997). This finding emphasizes the relevance of research on sleep and circadian rhythms in driving. The aim of the current research was to study the influence of several circadian and time-related factors (chronotype, time of day and time on task effects by controlling for prior sleep duration and prior wake) on performance during a simulated driving task.

Circadian rhythms set the timing for basic biological and physiological functions on a daily basis, such as sleeping and feeding, body temperature, hormone production and brain activity, thus influencing behavioral and cognitive functions (Berendes et al., 1960; Nathaniel Kleitman, 1933). Performance in cognitive tasks measuring simple reaction time (RT), attention and vigilance shows circadian rhythmicity, which indicates that the amount of prior wake and the time of day at which a task is accomplished are major influences (Blatter & Cajochen, 2007; Lim & Dinges, 2008; Valdez, Ramírez, García, Talamantes, & Cortez, 2010; Kenneth P Wright et al., 2002).

Time of day is a key factor in tasks demanding vigilance such as driving, as highlighted by statistics on traffic accidents (Di Milia et al., 2011; S Folkard, 1997). Specifically, traffic accidents occur most frequently when both body temperature and vigilance levels are at minimum, that is, around 3 to 5 am. Time of day effects in driving performance have also been demonstrated by laboratory experiments (Akerstedt et al., 2010; Baulk et al., 2008; Michael G. Lenné, Triggs, & Redman, 1997). However, most of these studies have not considered the negative impact that extending duration of prior wake exerts upon driving performance, which can be exacerbated at specific times of day when vigilance is low, for example at 4 am (Matthews et al., 2012).

Individual differences in profiles of circadian rhythmicity, i.e. "chronotype", can be another relevant factor for studies addressing time of day effects on cognitive and driving performance. The chronotype reflects inter-individual differences in the phase (or amplitude) of circadian rhythms, such as body temperature and sleep cycle (Adan et al., 2012; Kerkhof & Van Dongen, 1996). Morning-type people tend to wake up and to go to sleep earlier, and show more arousal and activity during the morning, than evening-type people. This tendency can be measured by a questionnaire (J. Horne & Östberg, 1976) and has been related to genetic factors (Katzenberg et al., 1998). Morning-type individuals also show optimal performance on many cognitive tasks in the morning, whereas evening-type

individuals show best performance in the evening. This interaction between chronotype and time of day is known as the “synchrony effect” (C. P. May & Hasher, 1998).

Chronotype has been acknowledged as a crucial factor in research on fatigue and accident risk (Di Milia et al., 2011). However, the influence of chronotype on driving performance remained to be tested. The few available evidence that measured chronotype has controlled rather than manipulated this factor by testing only participants with intermediate chronotype (Matthews et al., 2012)(Akerstedt et al., 2010)(Akerstedt et al., 2010). A recent study reported that morning-type participants showed higher cortisol levels (indicating higher arousal), reported both less subjective workload and reduced sleepiness than evening-type participants during a simulated driving task (Oginska et al., 2010). Unfortunately, however, the Oginska et al.’s study did not focus on driving performance so that measures related to the driving task were not reported. Therefore, the current study aimed to investigate the influence of chronotype on driving performance, by simultaneously considering time of day and prior wake factors.

Task duration (“time on task”) is another relevant factor influencing cognitive performance (Mackworth, 1948), and therefore the level of vigilance during driving. Many studies on real and simulated long driving have reported performance decrements, for example, by showing that the lateral position of the car becomes more variable (i.e., SDlat measure) and less accurate along time on task (e.g., Brookhuis & de Waard, 1993). The time on task effect has been related to increased fatigue and sleepiness, and to decrements in vigilance, which can be indexed by self-report and electroencephalographic (EEG) measures (Otmani, Pebayle, Roge, & Muzet, 2005; Ranney, Simmons, & Masalonis, 1999). For example, subjective sleepiness and EEG alpha activity have been shown to increase concomitantly with time on task (Kecklund & Akerstedt, 1993).

Given that vigilance fluctuates across time of day, it is reasonable to expect that the vigilance decrement during driving can be affected by time of day. This issue was addressed by a recent study, but no interaction between time of day and time on task was reported (Akerstedt et al., 2010). Since chronotype was not measured in this study, it is possible that variability due to individual differences in chronotype might have precluded the finding of clear interaction between time of day and time on task. Hence, the current study tested for the first time (as far as we know), whether the vigilance decrement during driving depends on chronotype and time of day. We have recently found that the vigilance decrement during a task measuring vigilance and response inhibition (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) can be prevented by testing morning-type and evening-type individuals at their respective optimal times of day (T Lara, Madrid, &

Correa, n.d.). Thus, we expected to extend this finding to a simulated driving task, in order to counteract the impairments in performance during long driving.

To summarize, the current study tested morning-type and evening-type participants performing a simulated driving task in morning and evening sessions. Effects of the manipulation of chronotype and time of day were additionally tested by measuring subjective activation (Timothy H. Monk, 1989), vigilance during the Psychomotor Vigilance Task (Dinges & Powell, 1985), and the slow alpha frequency range of the EEG (Kecklund & Akerstedt, 1993; Klimesch, 1999) before and during simulated driving. These variables were further analyzed by multiple regression (see Supplementary Material 2.2) in order to model and predict driving performance.

On the basis of the literature reviewed above, we expected to find a reduced vigilance decrement in driving performance when participants were tested at the optimal rather than non-optimal time of day according to their chronotype. We also predicted higher subjective activation, faster RTs in the PVT and lower alpha power in the EEG, at optimal compared to non-optimal times of day.

2. Material and methods

2.1. Participants

Twenty-nine participants with extreme chronotype were contacted from a database of students from the University of Granada who completed the Spanish reduced version of the Morningness-Eveningness Questionnaire (Adan & Almirall, 1991) to take part in the experiment voluntarily. Data from four participants were excluded from the study as they either crashed the car (two of them were driving at their non-optimal time of day) or missed one session. Data from eleven participants who either slept less than 6 hours the night prior to the experiment, did not complete any of the tasks or their EEG recording was excessively noisy, were replaced by testing new participants.

Summing up, data from twenty-five participants (age range 18-26 years old, Mean age = 21.09, SD = 2.46), all of them female, right-handed, with normal or corrected to normal vision, were finally included in the analyses. Testing only females was not particularly intended and was due to practical reasons regarding higher availability of this specific sample. There were no male participants in the rejected sample described above. Thirteen participants with scores of 17 and above were assigned to the morning-type group, whereas twelve participants with scores of 9 and below were assigned to the evening-type group. The study was conducted in accordance with both the ethical guidelines of the University of Granada and the standards laid down in the 1964 Declaration of Helsinki. Participants gave informed written consent before the study and they were rewarded with course credits for their participation.

2.2. Apparatus and Stimuli

Participants' body temperature was measured by means of an electronic thermometer placed under the armpit. The reduced version of the Spanish adaptation of the Morningness-Eveningness Questionnaire (rMEQ, Adan & Almirall, 1991; J. Horne & Östberg, 1976) was developed to measure participants' chronotype on the internet (available at <http://wdb.ugr.es/~molinae/rmeq/>). Scores in this questionnaire can range in a continuous between 4 (extreme eveningness) and 25 (extreme morningness). Subjective activation and affect were measured by an electronic version of the Visual Analogue Scale developed by Monk (1989). Scores can range from 0 (minimum activation/positive mood) to 100 (maximum activation/positive mood).

The simulated driving task and the PVT were run on the same PC laptop (Intel Core 2 Duo at 1.8 GHz with 2 GB of RAM, 15.6" LCD screen). The PVT task was programmed with E-Prime software (Schneider, Eschman, & Zuccolotto, 2001). The target stimulus was a black circle with a red edge (diameter: 9.15 degrees of visual angle at a viewing distance of 50 cm). As simulated driving task we used the Racer software (<http://www.racer.nl/>; version 0.8.9), which is free, customizable through ASCII files and it generates a log file on driving performance that can be analyzed with Matlab (Mathworks Inc.).

The track used in our study was the Speedest2 (<http://www.racer-xtreme.com/>), a road forming a big ovaled-rectangle (approximately 3,000 x 1,750 m, with a bend radius of 850 m), which was specifically selected to study time on task effects on vigilance by simulating monotonous driving on a highway. Sharp bends involving high driving skills were thus avoided. The car was a model of the Lexus IS350 to improve simulation of physical behavior in real conditions. The display showed a green line near the center of the track, and a velocity gauge on the bottom left corner of the screen (Figure 1, top). The car was controlled through a Logitech Momo Racing wheel and pedals set. Auditory feedback of the engine was provided through loudspeakers (Figure 1, bottom).



Figure 1. Display presented to the participant in the driving task (top) and experimental setup for the driving task (bottom).

Participants were instructed to drive the car following the green line drawn on the center of the road. The task involved keeping the car both as centered on the line as possible and at a constant velocity of 60 miles per hour (i.e., 96.56 km/h). The surface of the road was irregular, thus causing smooth but unpredictable deviations of the car position. Hence, the task demanded continuous attentional tracking of the car trajectory which participants had to correct with the steering wheel constantly. That is, they had to maintain attention both to the speed and position of the car.

EEG activity was recorded only during the simulated driving task with a 128-electrode net (Electrical Geodesics Inc.; Tucker, Liotti, Potts, Russell, & Posner, 1994). E-Prime was used to synchronize the driving task with the EEG data acquisition.

2.3. Procedure

Each participant completed identical 2-hour sessions in two consecutive days, one at 8 am and one at 8 pm. The time of day of the first session was counterbalanced across participants. At the beginning of the session, the experimenter registered the participant's amount of experience with both real driving and videogames, body temperature, amount of sleeping during the previous night, waking time and consumption of coffee or other stimulant substances during that day. Then, the participant completed the Monk's activation-affect scale, performed the PVT task for 10 minutes and a go no-go temporal orienting task (A. Correa, Triviño, Pérez-Dueñas, Acosta, & Lupiáñez, 2010) for another 10 minutes that was counterbalanced with the PVT (this task was part of another study to be reported elsewhere).

In the PVT task, participants were instructed to pay attention to the red empty circle and to press a key as soon as the circle started to fill up in red (in a counter-clock wise manner, and at an angular velocity of approximately 0.011 degrees per second), which happened every trial after a random interval ranging between 2 and 10 seconds. Participants were encouraged to respond as quickly as possible while avoiding anticipations.

After that, the electrode net was placed on the participant, who stayed five minutes with the eyes open and five minutes with the eyes closed, in order to measure the individualized alpha frequency (IAF). The IAF was used as an anchor point to calculate the different frequency bands. Then the driving task was administered for approximately one hour. The experimenter remained in the room while the participant drove the first straight of the circuit to ensure accomplishment of task instructions. Participants completed a lap in 3-4 minutes, and each participant completed a minimum of 9 laps (i.e., 18 hemi-laps). Finally, after the driving task, participants completed the Monk's activation-affect scale again.

2.4. Design and Data Analysis

The general design consisted of a repeated-measures analysis of variance (ANOVA) with Chronotype (morning-type, evening-type) as between-participant factor and Time of day (morning: 8am, evening: 8pm) manipulated within-participants. However, given that evening-type participants had slept significantly longer at the evening session (see details below in 3.1), the analyses focused on testing the effect of chronotype only in the morning session, and the effect of time of day only in the morning-type group, in order to control for the influence of prior sleep (Matthews et al., 2012). Further analyses of covariance (ANCOVA) tested for the synchrony effect on our main measures by including Prior sleep to the evening session as a covariate in the full Chronotype x Time of day design (see Supplementary Material 2.3).

The analyses of the PVT task included the median RT of responses above 100 ms, amount of anticipations (responses below 100 ms) and lapses (RTs above 500 ms). The design of the driving task additionally included Type of stretch (straight, curve) and Hemi-lap (1 to 15), which was used to study the effect of time on task (i.e., the vigilance decrement). Two additional hemi-laps were first completed as practice and were therefore not included in the analyses. The analysis of driving performance included the mean error in the position of the car corrected by the velocity. That is, we scaled the absolute values of the position error with an index of the velocity error, as difficulty of driving could vary with velocity. The velocity error was the absolute value of the difference between the instructed (60 miles per hour) and the actual velocity. The position error could take values

from -0.5 to 0.5, but was later rectified so that position error ranged from 0 to 0.5 (i.e., 0 meaning perfect execution). We also analyzed the standard deviation of the corrected position error (SDlat; see Supplementary Material 2.1), a measure commonly used in the literature (e.g., Akerstedt et al., 2010; Baulk et al., 2008; Matthews et al., 2012).

Electrophysiological activity was recorded from a 128-electrode Electrical Geodesics system, off-line preprocessed using FASTER (Nolan, Whelan, & Reilly, 2010), and then analyzed by Fast Fourier Transform using EEGLab (Delorme & Makeig, 2004). The band frequencies were defined in relation to the IAF following the method described by Klimesch (1999). We then focused in the lower alpha band, defined as the frequency between IAF minus 4 and IAF, on the cluster of electrodes with the highest activation on the alpha frequency band, located in posterior sites (see Supplementary Material 1, for further details on EEG methods).

Effect sizes of significant results in the ANOVA are reported as partial eta-squared (η^2), which quantifies the proportion of the variability in the dependent variable that is explained by the effect. The Greenhouse-Geisser correction was applied, and corrected probability values and degrees of freedom are reported, when sphericity was violated (Jennings & Wood, 1976).

3. Results and Discussion

3.1. Questionnaires

In the evening session, five participants (2 morning-type and 3 evening-type) reported having had a nap after lunch. Five participants (3 morning-type) drank coffee within the four hours prior to the morning session, and three of them (1 morning-type) drank coffee before the evening session. Thus, both nap and coffee intake were reasonable balanced for both chronotype and sessions.

The ANOVA of the rMEQ scores with Chronotype as between-participants factor confirmed that the morning-type group scored significantly higher in morningness ($M = 18.15$, $SD = 1.34$) than the evening-type group ($M = 9.17$, $SD = 0.83$), $F(1, 23) = 394.84$, $p < 0.001$, $\eta^2 = .94$. The two chronotype groups were matched in terms of age, number of years with driving license and experience with videogames (all $F < 1$). However, the ANOVA on the sleep duration in the night prior to the experiment ("Prior sleep") revealed a significant interaction between Chronotype and Time of day, $F(1, 23) = 6.66$, $p = .017$, $\eta^2 = .22$. Post-hoc Fisher LSD comparisons showed that evening-type participants slept longer in the night prior to the evening session ($M = 7.83$ hours, $SD: 1.11$) than: 1) evening-types before the morning session ($M = 6.46$, $SD = 0.50$), 2) morning-type participants before the morning session ($M = 6.58$, $SD = 0.53$), and 3) morning-types

before the evening session ($M = 6.96$, $SD = 0.78$), all $p < .01$. Importantly, participants in these three latter conditions were balanced in sleeping duration: morning-type morning-session compared to morning-type evening-session, $p = 0.16$; morning-type morning-session compared to evening-type morning-session, $p = .70$. Therefore, subsequent ANOVAs tested for the effect of Chronotype only in the morning session, and the effect of Time of day only in the morning-type group, whereas an ANCOVA including Prior sleep as covariate tested for synchrony effects as revealed by an interaction between Chronotype and Time of Day (ANCOVA results are described in Supplementary Material 2.3).

3.2. Effect of Chronotype in the morning session

The analysis on the amount of *time awake* before the morning session did not show significant differences between morning-type ($M = 1.15$, $SD = 0.32$) and evening-type ($M = 1.00$, $SD = 0.37$) groups, $F(1, 23) = 1.26$, $p = .27$. Similarly, body temperature in the morning session did not differ between morning-type ($M = 36.24$, $SD = 0.47$) and evening-type ($M = 36.49$, $SD = 0.44$) participants, $F(1, 23) = 1.80$, $p = .19$.

The Chronotype (morning-type, evening-type) x Pre-post (before driving, after driving) ANOVA on *subjective activation* in the morning session showed a significant main effect of Chronotype, $F(1, 23) = 9.88$, $p < .01$, $\eta^2 = .30$, such that morning-type reported higher activation ($M = 55.45$, $SD = 15.54$) than evening-type ($M = 38.06$, $SD = 11.65$) participants. The Pre-post effect was also significant, $F(1, 23) = 5.16$, $p = .03$, $\eta^2 = .18$, leading to reduced activation at the end ($M = 43.21$, $SD = 16.05$) as compared to the beginning ($M = 51$, $SD = 20.14$) of the session. The analysis on subjective affect did not show significant main effects or interactions (all $F < 1$).

The analysis of the *PVT performance* in the morning session did not show significant differences between chronotypes in terms of median RTs, lapses or anticipations (all $F < 1$).

The Type of stretch (straight, curve) x Chronotype (morning-type, evening-type) x Hemi-lap (1 to 15) ANOVA on the *mean position error* during the driving task in the morning session revealed a significant main effect of Hemi-lap, $F(3.36, 77.30) = 3.52$, $p = .02$, $\eta^2 = .13$. Specifically, the position error followed a significant linear increment across hemi-laps ($r = 0.89$, $p < .001$), that is, the vigilance decrement. Most relevant was the significant interaction between Chronotype and Hemi-lap, $F(3.36, 77.30) = 3.89$, $p < .01$, $\eta^2 = .14$ (Figure 2). Further analyses revealed that the vigilance decrement was present in the evening-type group ($r = 0.91$, $p < .001$), but it was absent in the morning-type group ($r = -0.14$, $p = .63$).

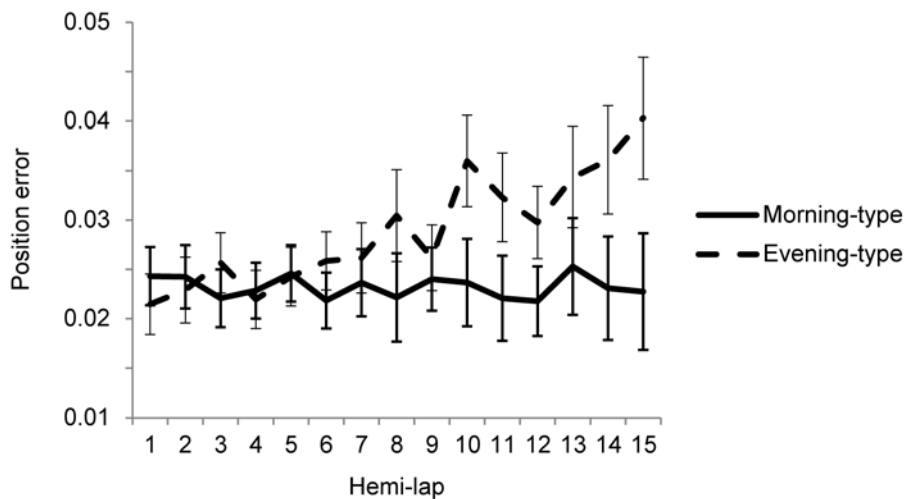


Figure 2. Mean position error (in distance units) as a function of Hemi-lap for morning-type (solid line) and evening-type (dashed line) groups driving in the morning session. Error bars represent the standard error of the mean.

The remaining effects were not close to the significance level (all $p > .2$), except for a marginally significant main effect of Type of stretch, $F(1, 23) = 3.75, p = .07$, suggesting that participants tended to drive more accurately in straights than in curves.

The analysis of **slow alpha** ($IAF - 4$ Hz to IAF Hz) frequency power during eyes closed did not show significant differences between chronotypes, $F < 1$. In the driving task period, the Type of stretch x Chronotype x Hemi-lap ANOVA on the slow alpha power revealed a main effect of Type of stretch, $F(1, 23) = 9.59, p < .01, \eta^2 = .29$, leading to higher alpha power on curves ($M = -1.69$) than on straights ($M = -1.91$), and a main effect of Hemi-lap, $F(3.67, 84.33) = 23.04, p < .001, \eta^2 = .50$, showing a significant linear increment of alpha across hemi-laps ($r = 0.96, p < .001$), which suggests a vigilance decrement. In contrast to the behavioral data, this decrement did not differ between chronotypes ($F < 1$; Figure 3). No other significant terms in the ANOVA reached statistical significance (all $p > .23$).

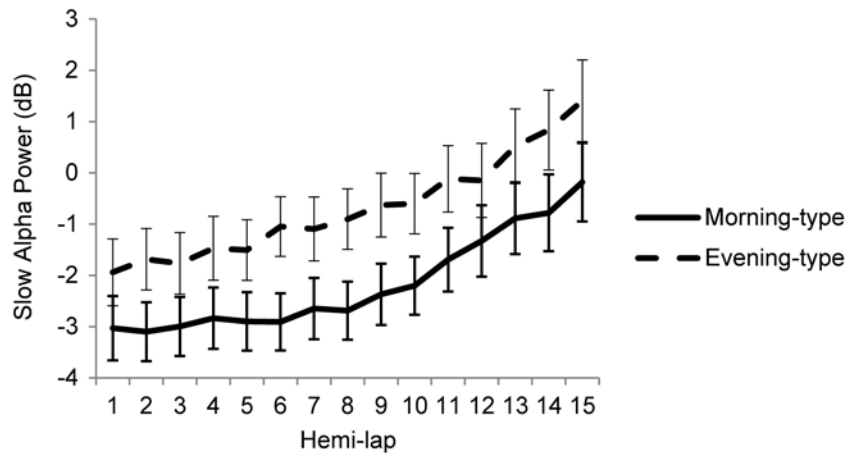


Figure 3. Mean slow alpha power (in dB) as a function of Hemi-lap for morning-type (solid line) and evening-type (dashed line) groups driving in the morning session. Error bars represent the standard error of the mean.

Altogether, the results of the morning session replicated the typical effects associated to the vigilance decrement by showing reduced subjective activation after driving, decreased accuracy and higher variability of the car position along hemi-laps (in the evening-type group), and linear increments in EEG alpha power as a function of hemi-lap (Brookhuis & de Waard, 1993; González, Kalyakin, & Lyytinen, 2009; Kecklund & Akerstedt, 1993; Otmani, Pebayle, et al., 2005; Ranney et al., 1999). The analyses further showed that morning-type and evening-type participants did not differ in terms of sleeping duration the night prior to the experiment, time awake, body temperature, vigilance as measured by the PVT and EEG alpha power. In contrast, the chronotype groups differed in both subjective activation and the vigilance decrement function related to driving performance. In the morning session, morning-type participants reported to be more active and indeed did not show any vigilance decrement as compared to evening-type participants, who could not attenuate it. This finding extends our previous research indicating that the vigilance decrement in attentional functions related to response inhibition as measured by the SART can be prevented by performing the task at the optimal time of day according to chronotype (T Lara et al., n.d.).

At first, the lack of chronotype differences in body temperature, PVT performance and alpha activity was unexpected on the basis of previous research (Adan et al., 2012), but it can be attributed to the balance of sleep duration and prior sleep between the

groups. In that sense, the simulated driving task was more sensitive to individual differences based on chronotype than the other measures of vigilance. The EEG data further showed that slow alpha activity followed a linear increment across the driving task, but it was not sensitive to the additional influence of chronotype.

3.3. Effect of Time of day in the morning-type group

The analysis on the amount of *time awake* confirmed that the morning-type group had spent less time awake between the waking-up time and the beginning of the morning session ($M = 1.15$, $SD = 0.32$) as compared to the beginning of the evening session ($M = 11.35$, $SD = 1.30$), $F(1, 12) = 938.42$, $p < .001$, $\eta^2 = .99$. Likewise, body temperature was lower in the morning ($M = 36.24$, $SD = 0.47$) compared to evening ($M = 36.55$, $SD = 0.53$), $F(1, 12) = 5.25$, $p = .04$, $\eta^2 = .30$.

The Time of day (morning, evening) x Pre-post (before driving, after driving) ANOVA on *subjective activation* showed a significant main effect of Time of day, $F(1, 12) = 8.40$, $p = .01$, $\eta^2 = .41$, such that the morning-type group reported higher activation in the morning ($M = 55.45$, $SD = 15.54$) than in the evening ($M = 43.25$, $SD = 14.29$). Similarly to results reported in Section 3.2, the Pre-post factor was significant, $F(1, 23) = 5.63$, $p = .04$, $\eta^2 = .41$. The analysis on subjective affect did not show significant main effects or interactions (all $p > .16$).

The *PVT* performance of the morning group did not show significant differences between morning and evening sessions in terms of median RTs, lapses or anticipations (all $p > .12$).

The Type of stretch x Time of day x Hemi-lap ANOVA on the *position error* during the driving task in the morning-type group did not show significant effects either with the mean (all $p > .15$) or the *standard deviation* (all $p > .12$).

Slow alpha power during eyes closed did not differ between morning and evening sessions in the morning-type group, $F < 1$. The Type of stretch x Time of day x Hemi-lap ANOVA on the slow alpha power during driving replicated the results described in 3.2, that is, a main effect of Type of stretch, $F(1, 12) = 13.75$, $p < .01$, $\eta^2 = .53$, and a main effect of Hemi-lap, $F(1.61, 19.32) = 13.78$, $p < .001$, $\eta^2 = .53$. None of the remaining terms in the ANOVA reached statistical significance (all $p > .15$).

To summarize, the analysis of the time of day effect in morning-type participants revealed stable performance across sessions in both the *PVT* and the driving task, although they reported to be more alert and body temperature was lower in the morning compared to the evening. In this group, the lack of a decline in driving performance in the evening session may have been achieved at the cost of higher effort and workload, as

previously suggested (Oginska et al., 2010). Although we did not measure subjective workload, this explanation is consistent with our finding of time on task effects on alpha EEG, suggesting that morning-type participants driving at their non optimal time of day also showed the typical neural consequences associated to the vigilance decrement. Another possibility considers that the evening session was not late enough to capture clear effects of time of day on behavior, as it fell within the “forbidden zone for sleep” or “wake maintenance zone”(between 8 and 10 pm), when the alertness level is particularly high (Lavie, 1986).

4. Conclusions

The current study tested for the first time the combined influence of chronotype and time of day on driving performance, and its evolution as a function of time on task, by controlling for the effects of sleeping duration and prior wake. The main finding showed a strong linear decrement in driving performance across time on task in evening-type participants, which was not present in morning-type participants. This result was found in the morning session, when both chronotype groups were tested under similar conditions, that is, at the same time of day and with balanced doses of sleeping duration and prior wake.

The main question then concerns the mechanisms underlying the differential driving behavior of morning-type compared to evening-type individuals. Different personality traits associated to chronotype can play a role, as evening-type participants usually show extraversion, low conscientiousness, high impulsivity and sensation seeking, which have been related to poor vigilance and increased accident risk (Di Milia et al., 2011; Finomore, Matthews, Shaw, & Warm, 2009). Previous findings of both higher arousal as indexed by cortisol level and reduced subjective workload in morning-type compared to evening-type participants when driving in the morning has been interpreted as differential appraisal of the simulated long driving task. This suggests that the task was more challenging and motivating for morning-type than evening-type participants (Oginska et al., 2010). Therefore, further research about the influence of both chronotype and personality factors on fatigue, accident risk and driving should help explain the bases of our main empirical finding (Di Milia et al., 2011).

The current study presented several limitations that should be addressed in future research. Despite the multiple inclusion criteria required to participate in the experiment, sleeping duration in the evening session could not be entirely controlled in the final

sample, thus making it difficult to analyze the data from evening-type participants in the evening session (the synchrony effect was nevertheless studied by means of analyses of covariance). This circumstance might be a normal consequence of testing under ecological free-living conditions as compared to more controlled experimental settings typically used in circadian rhythm research, such as procedures involving forced-desynchrony and the measurement of circadian variables during the week prior to the experiment (Matthews et al., 2012). Another aspect susceptible of improvement concerned the sample, which could have been larger and include male participants. It is not uncommon, however, to find studies focusing on one sex, male in this case (Matthews et al., 2012; Oginska et al., 2010), so we do not have strong reasons to expect different results as a function of sex in our experiment. We also focused on testing extreme chronotypes in order to optimize the finding of chronotype effects. Further research could also test intermediate chronotypes, who represent about the 60% of the population. Nevertheless, our selection criteria assured the balance of other several key variables for circadian research (see also Akerstedt et al., 2010; Oginska et al., 2010). Finally, we acknowledge that our study was limited to the use of a simulated driving task. The generalization of the current findings to real driving settings should be further supported by future experiments on the field and demographic studies (Di Milia et al., 2011) on the relationship between chronotype, time of day and traffic accidents.

To conclude, the current research contributes to further understanding of main circadian and time-related factors by emphasizing the relevance of chronotype, an understudied but influential variable with regard to performance in vigilance and driving tasks. The consideration of individual variability in chronotype in combination with time of day and sleep-related factors can provide practical implications for the design of work schedules to enhance human performance and prevent accidents during activities involving health risks. Future research on the interactive effects of circadian and sleep factors should inform the design of effective countermeasures to prevent declines in performance for tasks executed under non-optimal circadian conditions.

5. Acknowledgments

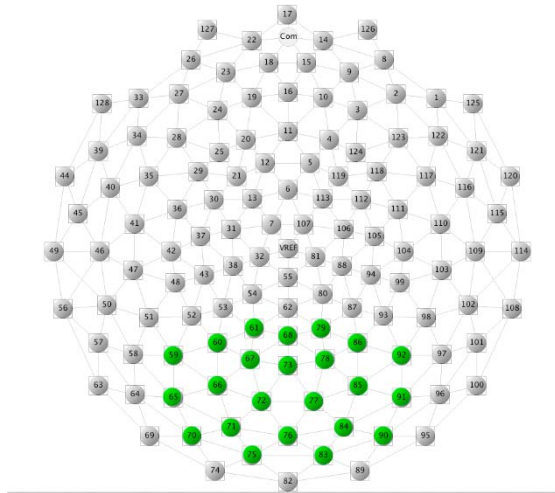
This work was supported by the Spanish Ministerio de Ciencia e Innovación (Ramón y Cajal programme: RYC-2007-00296, PLAN NACIONAL de I+D+i: research grant PSI2010-15399) to AC, by a predoctoral grant (FPI, MICINN) to EM, and by the Junta de Andalucía (research grant: SEJ-6414) to DS and AC. The authors are grateful to Dr. Juan Antonio Madrid and Dr. Mercedes Atienza for their helpful advice on the design and analysis of this research.

Supplementary Material.

“Effects of chronotype and time of day on the vigilance decrement during simulated driving”.

1. Supplementary Methods

Electrophysiological activity was recorded from 128 electrodes referenced to the vertex. The electrodes located above and beneath the eyes, and to the left and right of the external canthi of the eyes were used to detect blinks and eye movements. The EEG net was connected to an AC-coupled high-input impedance amplifier (200 M Ω), and impedances were kept below 50k Ω , as recommended for the Electrical Geodesics high-input impedance amplifiers. While registering, the signal was amplified, filtered (0.1 to 100 Hz band pass) and digitized with a sampling rate of 250 Hz using a 16 bits A/D converter. EEG data from all periods (eyes opened, eyes closed and driving) was off-line preprocessed using FASTER version 1.2.3. (Nolan et al., 2010). Data were re-referenced to average and band-pass filtered between 0.5 and 40 Hz. Before epoching, bad channels were interpolated. Data were divided in 4-second epochs. A new interpolation of bad channels within each epoch was performed. The continuous EEG frequency power in the alpha band was analyzed by Fast Fourier Transform of 256 points using EEGLab software (Delorme & Makeig, 2004). The band frequencies were defined in relation to the IAF following the method described by Klimesch (1999). We analyzed the power of the eyes-closed period in two posterior electrodes, O1 and O2. The average power of those two channels was then used to find the peak between 9 and 12 Hz for each subject and session. This peak was defined as the IAF for that subject in that session. We then focused in the lower alpha band, defined as the frequency between IAF minus 4 and IAF. After averaging data from all participants, a channel spectra map was then generated for the eyes-closed period, which was used to select the cluster of electrodes with the highest activation on the alpha frequency band. This cluster comprised the posterior region of the brain on both hemispheres (Figure 2). We used this cluster for all the analyses.



Supplementary Figure 1. Electrode location of the 128-channel net. Green electrodes represent the cluster chosen for the EEG analyses during the simulated driving task.

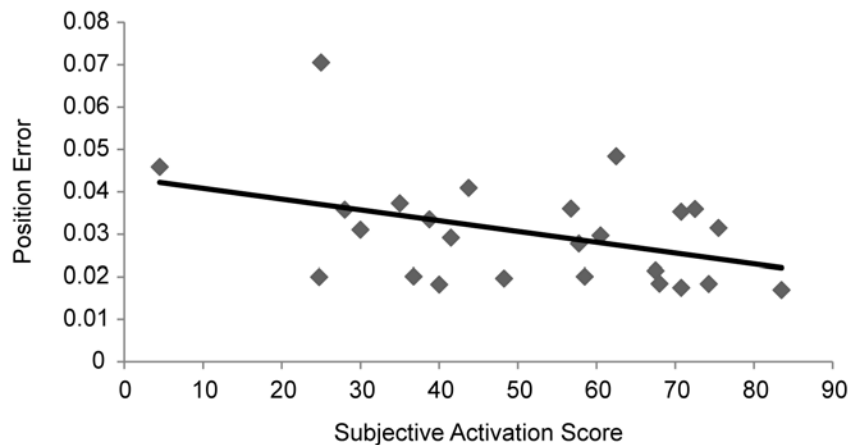
2. Supplementary Results

2.1. Effect of Chronotype in the morning session: Analysis of the standard deviation of the position error.

The Type of stretch x Chronotype x Hemi-lap ANOVA on the *standard deviation of the position error* replicated the pattern of results described above for the mean position error. That is, we found a significant main effect of Hemi-lap, $F(4.33, 99.63) = 2.83, p = .03, \eta^2 = .11$, and a significant interaction between Chronotype and Hemi-lap, $F(4.33, 99.63) = 2.54, p = .04, \eta^2 = .10$, which revealed increasing variability of driving performance across time on task (i.e., the vigilance decrement) only for evening-type but not morning-type participants. The main effect of Type of stretch, $F(1, 23) = 6.58, p = .02$, showed higher variability of driving performance in curves than in straights.

2.2. Multiple regression analysis in the morning session.

A multivariate stepwise regression analysis was performed to predict mean error position of driving performance in the morning session, which included rMEQ scores, subjective activation and affect before the driving task, RT performance in the PVT and alpha power during driving. A significant model was obtained, $F(1,23) = 4.34, p = .049$, which included subjective activation (beta = $-.41, R^2 = .16, \text{adjusted } R^2 = .13$) as the only significant predictor. As can be observed in Figure 5, higher scores of self-reported activation just before the driving task were associated to lower position errors in driving performance.



Supplementary Figure 2. Mean position error plotted against scores of subjective activation before the driving task in the morning session.

The regression analysis did not find a correlation between slow alpha EEG and driving performance, which did not confirm our hypothesis based on previous research (Akerstedt et al., 2010; Kecklund & Akerstedt, 1993; Lal & Craig, 2002), but it is consistent with other studies (Otmani, Pebayle, et al., 2005). The behavioral measures provided by the PVT were not able either to reliably predict driving performance in our experiment, which suggests that simple RT short tasks are not sufficient to predict performance of complex tasks like driving (Baulk et al., 2008; Jackson, Croft, Kennedy, Owens, & Howard, 2012; Matthews et al., 2012). On the other hand, subjective activation showed a significant correlation with driving performance, which is congruent with multiple studies (Akerstedt et al., 2010; Ingre, Akerstedt, Peters, Anund, & Kecklund, 2006; Otmani, Rogé, & Muzet, 2005; Reyner & Horne, 1998). The fact that the correlation was rather weak and it did not explain much variance in the data could be improved by increasing sample size.

2.3. Analysis of the synchrony effect by ANCOVA

The analysis including prior sleep to the evening session as a covariate revealed a synchrony effect on *subjective activation* which was reflected by a significant interaction between Chronotype and Time of day, $F(1, 22) = 17.72, p < .001, \eta^2 = .45$. Planned comparisons showed that the morning-type group reported higher activation in the morning ($M = 55.45, SD = 19.86$) than in the evening ($M = 41.85, SD = 19.69$), $F(1, 22) = 8.59, p < .01$. In contrast, the Evening-type group reported higher activation in the evening

($M = 53.92$, $SD = 20.58$) than in the morning session ($M = 40.23$, $SD = 20.76$), $F(1, 22) = 10.96$, $p = .003$.

The ANCOVA on the reaction time data from the PVT also confirmed the synchrony effect by a significant interaction between Time of day and Chronotype, $F(1, 22) = 12.35$, $p = .002$, $\eta^2 = .36$. Planned comparisons in the evening-type group showed that RT was slower in the morning ($M = 309$, $SD = 39$) than in the evening ($M = 287$, $SD = 30$), $F(1, 22) = 13.36$, $p = .001$. No significant difference was found for the morning-type group, $F(1, 22) = 2.30$, $p = .14$.

Most relevant was the finding of synchrony effects on the vigilance decrement during driving performance as revealed by a significant interaction between Time of day, Chronotype and Hemi-lap, $F(3.32, 73.09) = 3.00$, $p = .002$, $\eta^2 = .18$. Further analyses revealed a significant interaction between Chronotype and Hemi-lap in the morning session, $F(3.34, 73.53) = 4.31$, $p < .01$, $\eta^2 = .16$, but not in the evening session, $F(3.16, 69.60) = 1.24$, $p = .30$.

The ANCOVAs on the alpha EEG data did not reveal any significant results (all $p > .1$).

To sum up, covariate analyses further confirmed the finding of a synchrony effect in driving performance, indicating that the vigilance decrement can be counteracted by driving at the optimal time of day according to the chronotype.

Estudio II y III

Electroencephalographic and peripheral temperature dynamics during a prolonged psychomotor vigilance task

1. INTRODUCTION

Road accidents caused by driver's fatigue are a main concern in road safety. Accident frequency has been shown to increment with the time driving (i.e., time on task), especially when driving on a monotonous road (S Folkard, 1997). In such monotonous environment, a decrement in attention leads to a higher risk of accidents. Thus, a substantial goal in psychological research is to develop neurophysiologically based models of fatigue and attention to prevent them.

To attain this goal, research has focused on, first, finding sensitive indices of the fluctuations of attention, and second, developing a model based in these indices that can anticipate such fluctuations. One of the most used indices is the electroencephalogram (EEG), especially the analysis of the EEG power spectra, whose fluctuations have been linked with attention and time on task long ago (Jung, Makeig, Stensmo, & Sejnowski, 1997). Thus, a wealth of literature has assessed the relationship between EEG and driving performance (e.g., Lal & Craig, 2002; Otmani, Pebayle, Roge, & Muzet, 2005; Perrier et al., 2016) showing that the monitoring of drivers' EEG can be a reliable method to predict attention fluctuations while driving. Moreover, the EEG frequency dynamics have been used to develop models that could predict the driver's attentional state on real time.

Among the techniques used to build these models, machine-learning algorithms have obtained the highest rates of accuracy (Davidson, Jones, & Peiris, 2007; F.-C. Lin et al., 2012; Ting, Hwang, Doong, & Jeng, 2008a). The typical paradigm consists of recording the participant's EEG while driving and then use these data to train a neural network that will build the model. Then, to test the accuracy of the resulting model, part of the data is fed to the neural network and the output is compared with the real outcome. A main drawback of these techniques is the need for big datasets to train the model (Liu, Lin, Wu, Chuang, & Lin, 2016). Moreover, most of these models are computed and customized for every subject (Chin-Teng Lin, Shu-Fang Tsai, & Li-Wei Ko, 2013; C.-T. Lin et al., 2006), which means that a long driving session per subject is needed to obtain his/her model. It is not clear, either, to what extent these models are subject- or task-specific. But the need to obtain models that can be applied to many different tasks is becoming an important request nowadays, where the need for monitoring the effects of fatigue become

crucial in many work environments. Moreover, as the applications of such models become wider, it is also important to obtain them from reduced datasets that can be obtained on the fly.

There have been hitherto a few attempts to transfer such a model between tasks. For example, Touryan et al. (2014) were able to transfer a regression model between two tasks, a perceptual discrimination task (i.e., RSVP), and a model developed from EEG data recorded during a driving task. To do so, the EEG log power spectra was used as predictor of performance in each task, by means of a linear regression model. This model was customized for every subject (i.e., electrode subset and regression coefficients were chosen for every subject in order to maximize the fit of the model) and then applied to the results of that specific subject in the other task, and the correlation between the predicted and the actual outcome was used as metric to evaluate the accuracy of the model. Results showed that the model could be transferred in either way (i.e., from one task to another or vice versa) between tasks for some subjects, but not for all. This was interpreted as a promising result to obtain a transfer model between tasks. However, a 60 minute data recording for both the driving task and the RSVP, was still necessary to construct the model. An alternative and challenging approach would be to obtain this model from a different, shorter and simpler task, and then apply it to the more complex driving task.

An excellent task candidate to construct the model described above is the Psychomotor Vigilance Task (PVT). The PVT (Basner et al., 2018; Dinges & Powell, 1985) is a straightforward and reliable tool for measuring fatigue in humans. In the PVT, participants have to respond, as fast as possible, to a simple visual stimulus. The inter-trial interval is randomly distributed between 2 and 10 seconds, and feedback of performance is displayed. The monotonous and unpredictable target presentation in the PVT makes subjects highly prone to lapses of attention. Moreover, the PVT has minimal learning effects, minimizing the variability due to participants' different ability and experience (Basner & Dinges, 2011). The PVT has been used to assess how different brain dynamics indices are affected by attention fluctuations, like evoked potentials (Käthner et al., 2014), frequency analyses (Chua et al., 2012a; Hoedlmoser et al., 2011) and fMRI (Drummond et al., 2005).

In this study we aimed, firstly, to obtain attention-related EEG indices from a simple, widely used, vigilance task as the PVT. And, second, to build a linear regression model based on such indices from the PVT to predict performance in a driving task. More specifically, in Experiment 1, we assessed the relationship between performance in a 45-min PVT and two psychophysiological measures: The skin temperature and the dynamics of EEG frequency power in three main bands (theta, alpha and beta), to identify the best predictors of attentional fluctuations in this specific task. In Experiment 2 we used such predictors obtained from a 20 min PVT to build a model of performance in a more complex simulated driving task.

2. GENERAL METHODS

2.1. Apparatus

2.1.1. Chronotype questionnaire

An online version of the rMEQ was developed to measure participants' chronotype (available at <http://wdb.ugr.es/~molinae/rmeq/>). Scores in this questionnaire fall into the interval between 4 (extreme eveningness) and 25 (extreme morningness).

2.1.2. The Psychomotor Vigilance Task

The PVT was run on an Intel Core 2 Duo PC and a 17" CRT screen with a 60 Hz refresh rate, using E-Prime software (Schneider et al., 2001). The target stimulus was a black circle with a red edge (diameter: 9.15 degrees of visual angle at a viewing distance of 50 cm). Participants were instructed to pay full attention to the red empty circle, and press the space bar key with the forefinger of their dominant hand as soon as the circle started to fill up in red, which happened on every trial after a random interval ranging between 2,000 and 10,000 ms in a counter-clock wise manner, and at an angular velocity of approximately 92.3 degrees per second. Participants were instructed to respond as quickly as possible, while avoiding anticipations. Feedback was provided by displaying the RT for 500 ms after the participant's response (see figure 1).

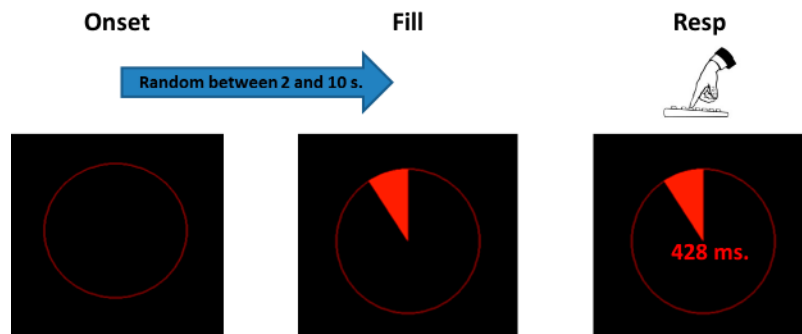


Figure 1. Sequence of event in the Psychomotor Vigilance Task

2.1.3. EEG recording

Electrophysiological activity was recorded from a 128-channel Geodesic Sensor Net of 129 Ag/AgCl electrodes [Electrical Geodesics, Inc. (EGI)], referenced to the vertex. The electrodes located above and beneath the eyes, and to the left and right of the external canthi of the eyes were used to detect blinks and eye movements. The EEG net was connected to an AC-coupled high-input impedance amplifier (200 M Ω), and impedances were kept below 50k Ω , as recommended for the Electrical Geodesics high-input impedance amplifiers. While recording, the signals were amplified, filtered (0.1 to 100 Hz band pass) and digitized with a sampling rate of 250 Hz using a 16-bit A/D converter.

2.2. Data analyses

2.2.1. PVT data analysis

The RT from the PVT was used as the behavioral measure. RTs faster than 100 ms (less than 1% of the trials) and anticipations were excluded from the analyses (cf. Basner & Dinges, 2011).

2.2.2. ICA analyses

Using EEGLAB v.12 (Delorme & Makeig, 2004) running under Matlab 7.5 [MathWorks, Inc.; <http://www.mathworks.com/>], continuous EEG data were first re-referenced to the average, high pass filtered at 1 Hz, low pass filtered at 40 Hz and six EOG channels were excluded from the analysis. Independent Component Analysis was used to decompose multi-channel EEG data into spatially fixed and

temporally independent components (ICs) through the extended infomax option of runica algorithm from the EEGLAB toolbox (Bell & Sejnowski, 1995; S Makeig, Jung, Bell, Ghahremani, & Sejnowski, 1997). A first ICA run was used to clean blinks and eye movements from the data. Then a manual inspection was performed, and non-stationary noise and bad channels were removed from the data. Finally, a second ICA run separate the source components from the EEG channels. ICA assumes that scalp EEG signals are a weighted linear mixture of electrical potentials projected instantaneously from distinct independent brain sources (Scott Makeig, Bell, Jung, & Sejnowski, 1996).

The spatial origin of every IC (i.e., the equivalent dipole) was localized using the DIPFIT2 routine (Oostenveld & Oostendorp, 2002). ICs with a residual variance of dipole fitting to the scalp map exceeding 15%, and ICs with dipoles located outside the brain were excluded from further analysis (Onton & Makeig, 2009). The estimated dipole locations were co-registered to an average brain model (Montreal Neurological Institute) and to obtain a better alignment to the model, the channels were manually warped (i.e. spatially adjusted) to a 10-20 electrode system.

To obtain comparable ICs across subjects, components were semi-automatically grouped into clusters using the EEGLab standard K-means clustering method (Makeig et al., 2002; Onton & Makeig, 2006), based on the ICs scalp maps, dipole locations and the power spectra of component activations. Although the clustering algorithm tries to assign one component from every subject to every cluster, that is not always possible, resulting in a different number of trials per cluster.

The EEG data were epoched around the target event, spanning 2 seconds before and 2 seconds after this event, and power spectra were calculated using a zero-padded FFT with Hanning tapers. Two types of analyses, phasic and tonic EEG dynamics, were performed for every cluster of interest.

Phasic EEG analyses

First, we computed the event related spectral perturbation (ERSP) between 2 and 30 Hz locked to the target (Makeig, 1993), in a 4 s window (2 s pre-target and 2 s post-target). The median RT from all the trials was also calculated and plotted for descriptive purposes, in order to depict the spectral perturbations related to both, the target and response events on every cluster.

The phasic analyses plots show the evolution of power in individual frequency bands with respect to the optimal alert state of every subject. To do so, we baselined data from every subject separately using its own pre-target power spectra from the short-RT trials (defined as trials within the 10% fastest reaction times for every subject (see Basner, Mollicone, & Dinges, 2011). The reason to baseline each subject using its own 10% fastest trials, was to assure obtaining frequency power deviations related to the best performance of each one. Then, we combined all trials from all subjects sorted by RT, making a new baseline correction using the overall 10% fastest RTs (just for clear representation purposes), and obtained an erp-image plot of the power for theta (4-8 Hz), alpha (8-12 Hz) and beta (12-20 Hz) frequency bands on a trial-by-trial basis, obtaining thus the EEG dynamics within the epoch and along the task (see Delorme et al., 2007 for a similar analysis). Target onset and RT are also represented on the plots.

To test for significant power deviations a non-parametric bootstrap statistical analysis was performed (Grandchamp & Delorme, 2011). For every frequency, an empirical distribution of the pre-target power in the 10% short-RT from all trials was constructed by resampling 10,000 times from the original data. From this distribution, we obtained a 95% confidence interval, whose 2.5 and 97.5 percentiles were used as a threshold for significance. Thus, data with a power value outside the confidence interval was considered a significant power change for that frequency. All non-significant data samples were assigned a power value of 0 in the plot, and therefore, were represented in green. A false discovery rate (FDR) correction was applied to all statistical results.

Tonic EEG analysis

To assess frequency power changes from high to low levels of vigilance, the power was analyzed only in the pre-target data. For every trial, we obtain the average power value from the 2 s pre-target segment. Then, the same baseline used in the phasic analyses (i.e., the average frequency power from the 10% fastest trials) was applied for every trial on every subject. Finally, all trials were sorted according to the RT for every individual frequency from 2 to 30 Hz.

The tonic plots represent the pre-target data plotted in the left column averaged for every frequency band (i.e., averaged from 4 to 8 Hz for theta, from 8 to 12 for alpha and from 12 to 20 for beta). See also Huang et al. (2009).

To assess significance, we applied the same non-parametric approach used in the phasic analyses to data in the 2 s pre-target windows.

3. EXPERIMENT 1

The PVT was designed to be sensitive to the homeostatic pressure for sleep, and has been mainly used in sleep deprivation and circadian rhythm studies (see Lim & Dinges, 2008, for a review; Correa, Molina, & Sanabria, 2014) because the fluctuations of attention over time are most evident with sleep deprivation.

Therefore, when the participants' arousal is relatively within the normal range (i.e., without sleep deprivation), performance in the PVT might be more stable across time related to subjects with sleep deprivation, and thus, an extended PVT like the one used in the present research (45-min long), could be necessary in order to study slowly-varying (tonic) shifts in non-sleep deprived participants' EEG.

Independent component analysis (ICA) was used to identify maximally independent neural processes and to model the fluctuations of the EEG related to fluctuations on performance. ICA can effectively obtain independent components (ICs) accounting for neural signals and artifacts such as eye movements and muscle noise (Debener et al., 2005; Delorme et al., 2007; Onton, Delorme, & Makeig, 2005). The use of ICA together with a dipole-fitting approach enabled us to identify the brain regions involved in the vigilance fluctuations during performance of the PVT.

Experiment 1 also measured skin body temperature as an additional physiological index of vigilance performance. Recent studies have linked fluctuations of body peripheral (skin) temperature to vigilance. Three skin temperature measures are typically assessed: Distal temperature (measured on distal extremities, like the wrist), proximal temperature (measured near the upper-body, for example under the clavicle) and the difference between distal and proximal temperature values, i.e., the distal to proximal gradient (DPG) measure. Romeijn and Van Someren

(2011) used a modified PVT demanding fine perceptual detection and found that increments of proximal (chest) and distal (finger) temperatures were related to both decrements in response speed and more lapses, while no effect was found for wrist temperature. Likewise, they found that an increment in the DPG between finger and chest resulted in a decrement of speed and an increment of lapses. Nonetheless, the relationship between temperature and performance in a long PVT has not been evaluated yet, and although the relationship between non-central temperature measures and sleepiness remains unclear, it has been proposed the DPG temperature as the optimum measure to assess this relationship (see Romeijn et al., 2011).

In Experiment 1, we hypothesized that RT increments in the PVT would be related to increment in the power of theta and alpha frequency bands on areas involved in the sustained attention network (i.e., parietal and right frontal areas). We also expected to find a positive correlation between the DPG and the RT (i.e., the higher the gradient temperature, the slower the responses to the PVT).

3.1. Participants

Seventeen female students from the University of Granada (age range 19-28 years old, Mean age = 21.72 years old, Standard deviation = 2.50 years old) participated in the experiment voluntarily in exchange of course credits. All participants had an intermediate-type chronotype according to the Spanish reduced version of the Morningness-Eveningness Questionnaire (rMEQ; Adan & Almirall, 1991) and reported at least 7 hours of sleep in the previous night ($M = 8.35$; $SD = 0.70$). They were all right-handed, with normal or corrected to normal vision. The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Participants gave informed written consent before the study and they were rewarded with course credits for their participation.

3.2. Apparatus and Stimuli

Body temperature was measured using a temperature sensor (iButton- DS1921H; Maxim, Dallas), which has a temperature range from $+15^{\circ}\text{C}$ to $+46^{\circ}\text{C}$ and 1°C of accuracy with a resolution of 0.125°C . The sensors were programmed to sample every minute along the experimental session.

3.3. Procedure

Each subject completed a one-hour length experimental session either at 11 am or 1 pm. Two sensors, one placed in the infraclavicular area of the chest and one in the ventral part of a wristband were used to measure proximal and distal temperature, respectively. Both sensors were placed on the non-dominant side of the subject before the start of the PVT, which was followed by a 10-minute acclimation period. During this time, participants completed the online version of the rMEQ, and were also asked about the amount of sleep during the previous night, the waking time, and whether they have had coffee or any other stimulant during that day. Finally, the electrode net was then placed and the PVT was performed for 45 minutes.

3.4. Data Analysis

To assess the relationship between temperature and performance (e.g., RT), generalized linear mixed effects models (GLMM) were used (Jiang, 2007). The GLMMs approach has been suggested to cope with problems related to non-normality of RT while avoiding the problems induced by an inverse transformation of the RTs due to “scale dependent” interactions (Lo & Andrews, 2015; Loftus, 1978). Three models were constructed for each temperature measure (i.e., distal, proximal and DPG). Every model included time-on-task (in order to isolate its effect from the attentional fluctuations). Thus, we had temperature and minute as fixed effects factors, and RT as the outcome variable. In order to match the sampling rate of the temperature measuring device, RTs from every minute were averaged. As random effects we had intercept for subject, as well as by-subject random slope for the effects of temperature and minute. Significance of the model was calculated based on likelihood ratio test of the full model against the model without the effect in question. All calculations were performed in Matlab R2015b [MathWorks, Inc.; <http://www.mathworks.com/>], using the generalized linear mixed-effects model class.

3.5. Results

All subjects had an intermediate chronotype (mean rMEQ score: 13, SD: 1), and slept at least for 7.5 h during the night before the experiment. The mean time

awake was 1.97 hours (SD: 0.68). None of the subjects reported having had coffee any time before the experiment.

3.5.1. Behavioral data

Figure 2 (left panel) shows the histogram of all participants' RT in the PVT. The distribution is left skewed with a mean of 380 ms and a standard deviation of 98 ms. There were a 91% of the RTs below 500 ms, which is the minimum RT to define a trial as a 'lapse' (Dinges et al., 1997). The 10% fastest trials had a maximum RT of 292 ms. In the right panel of figure 2, the evolution of mean RT along time on task is plotted, showing a positive linear trend between RT and minutes on task.

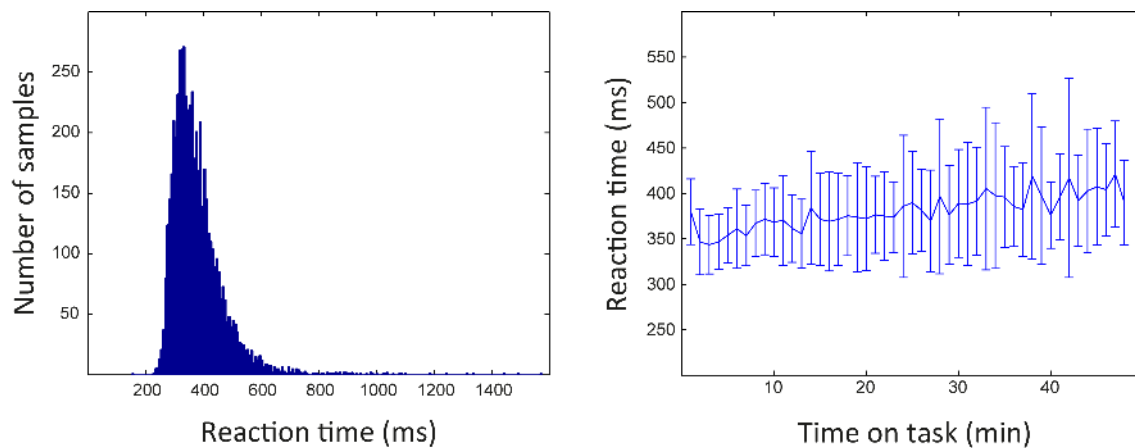


Figure 2. Distribution of RT (left) and evolution of RT with time on task (right) registered on the PVT. Error bars denote standard deviation.

3.5.2. Temperature and RT analysis

The generalized mixed effect models showed a significant positive relationship between RT and Distal (Effect = 10.21; SE = 2.81; $p = .011$) and DPG (Effect = 7.92; SE = 3.22; $p = .036$) temperature measures, that is, when Distal and DPG were higher, subjects were slower in their responses (see figure 3). No significant effect was found for Proximal temperature ($p = .106$).

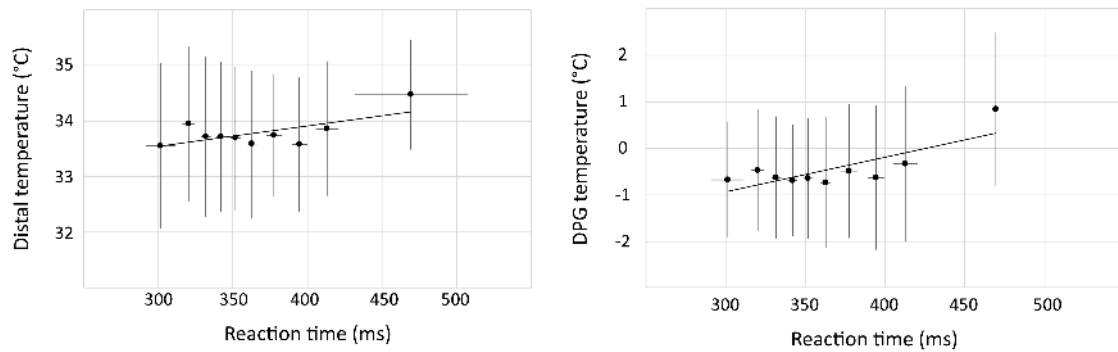


Figure 3. For descriptive purposes, RT data has been averaged in 10 percentiles and plot against temperature data (distal and DPG). Error bars represent standard deviation for RT (horizontal) and temperature (vertical). A trend line is also represented. Note that statistical analyses have been conducted on raw data..

3.5.3. EEG dynamics

From the resultant clusters obtained after grouping ICs, six clusters (i.e., left and right frontal, left and right parietal, premotor and central) were selected for further analyses based on previous literature (Chuang, Ko, Jung, & Lin, 2014; Drummond et al., 2005; Lin et al., 2010). Average Talairach coordinates for these clusters are, respectively, (-38, 44, 13), (-4, 17, 54), (28, 47, 18), (-22, -62, 0), (-7, -15, 25), (25, -52, 16), comprising the medial frontal gyrus, cingulate gyrus, left lingual gyrus, supplementary motor area and posterior cingulate cortex, regions related to the default mode network (DMN) and the fronto-parietal attention network (Hinds et al., 2013; Raz & Buhle, 2006; Weissman et al., 2006). Figure 4 shows average scalp maps (top) and dipole localizations (bottom) for these clusters. Note that dipole source location cannot be as accurate as neuroimage techniques, and locations obtained should be interpreted with caution.

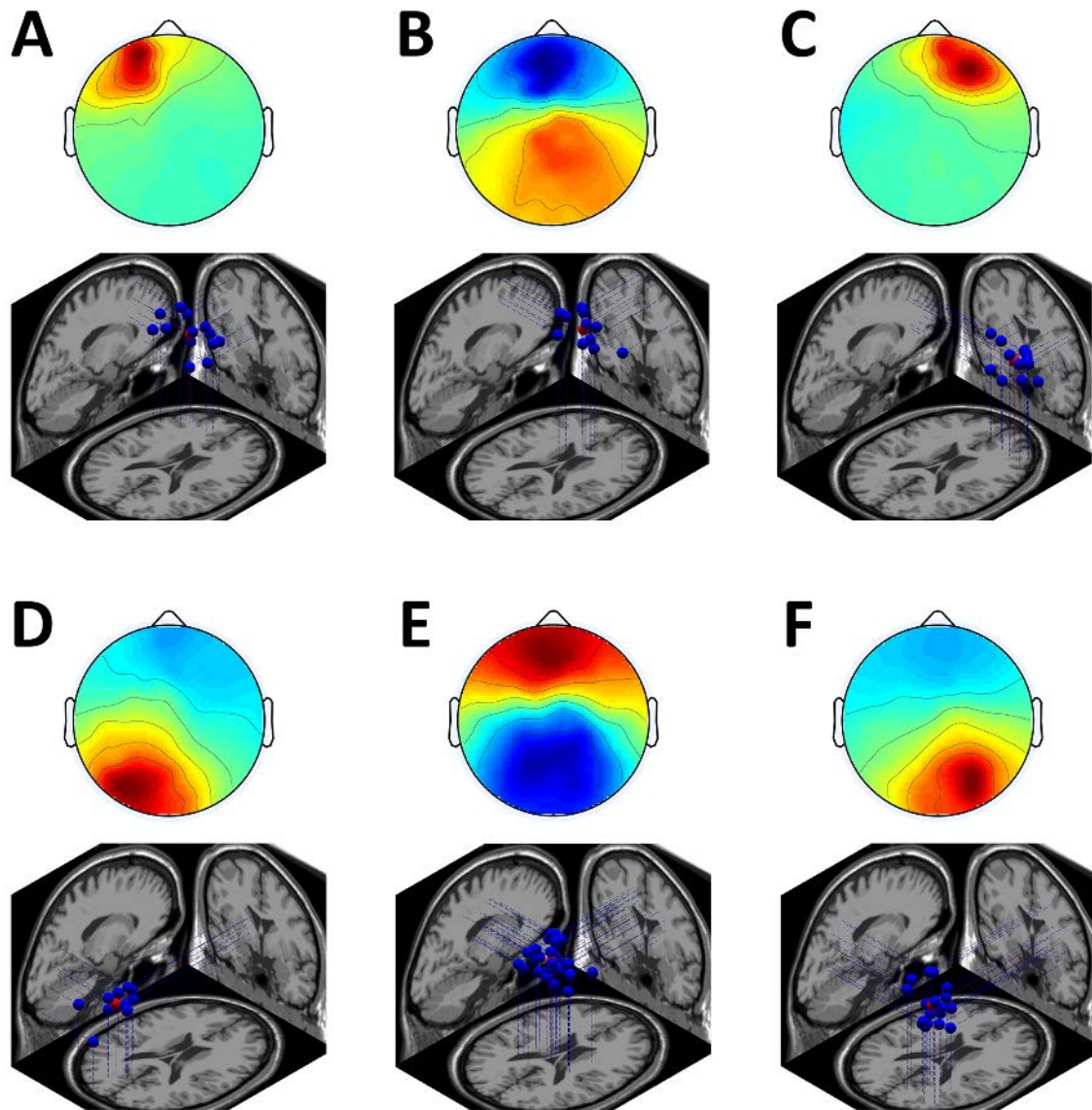


Figure 4. Average scalp maps and their corresponding dipoles obtained after grouping comparable ICs from all the subjects. Left frontal (A) and right frontal (C), premotor (B), central ϵ and left parietal (D) and right parietal (F) IC clusters were analyzed.

3.5.4. Phasic EEG dynamics

Figure 5 shows the phasic power spectra for the six clusters of interest. Left most images are the event related spectral perturbation (ERSP) time-locked to the target onset (dashed black vertical line). The median RT is represented by the solid black vertical line. The three images to the right are the RT-sorted ERSP images for

the theta, alpha and beta frequency bands. The solid black curve represents the RTs of all the trials.

The left and right parietal, central and right frontal clusters exhibited a theta burst after the target onset. This event-related synchronization (ERS) was time-locked to the target, and it was delayed around 100-150 ms in the central and frontal clusters. In the premotor cluster, theta was exclusively time-locked to the response, and synchronized around 100 ms before it. Finally, around 300-400 ms after the response, the theta synchronization disappeared for all clusters.

In the right frontal cluster, alpha showed an ERS around 200 ms after the target onset which vanished after the response. Alpha power also showed an event-related desynchronization (ERD) time-locked to the response in the right parietal, central and premotor clusters. This desynchronization immediately followed the response in the parietal and central clusters, and was delayed and less intensive in the premotor cluster.

Beta band showed an ERS time-locked to the target for the right frontal cluster and a similar behavior to alpha power in the parietal, central and frontal clusters, i.e., an ERD time-locked to the response for the parietal and central (although lower in intensity).

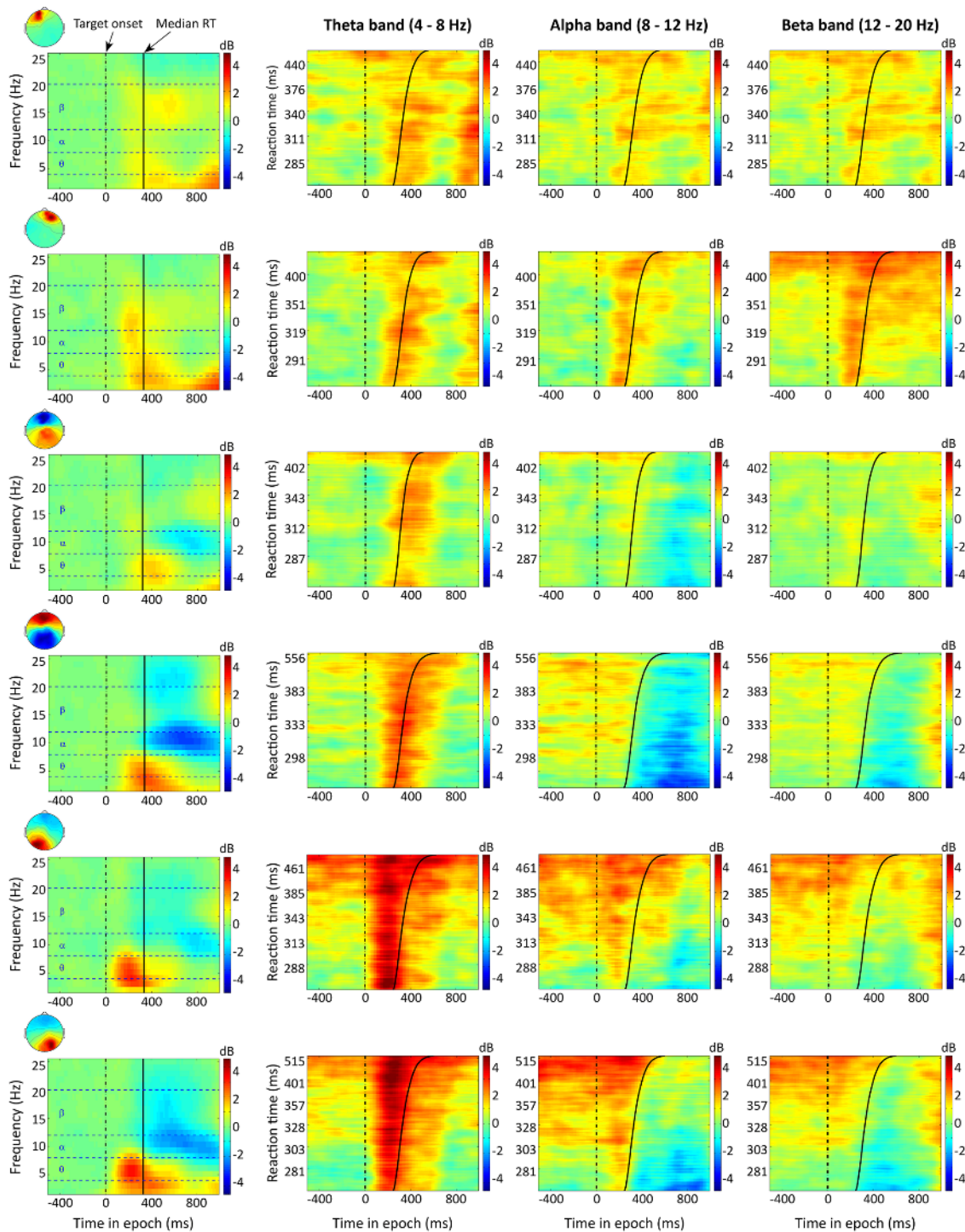


Figure 5. Phasic EEG dynamics for all clusters of interest. ERSP images (left) show the trial-averaged EEG changes in the epoch with respect to the baseline for every frequency. The three most right plots show the frequency power changes in the epoch across trials, which are sorted by RT, for theta, alpha and beta bands respectively.

3.5.5. Tonic EEG dynamics

Figure 6 shows tonic changes related to the baseline in spectral power for the six clusters of interest. The left image of every cluster shows how the mean power changes with RT for all frequencies. The three plots to the right focus on the averaged mean power for each frequency band (theta, alpha and beta). Statistical significant changes ($p < .05$) from the short-RT trials are represented on the left plots with colors other than green, and with a red horizontal line on the right plots.

In general, theta, alpha and beta bands increased with RT for all clusters except the premotor cluster, reaching a plateau for RTs greater than 500 ms. This increment was steeper in both the left and right parietal clusters, and also in the right frontal cluster for the beta band only. In the premotor cluster, the significant power increment for all frequency bands started at RTs greater than 400 ms.

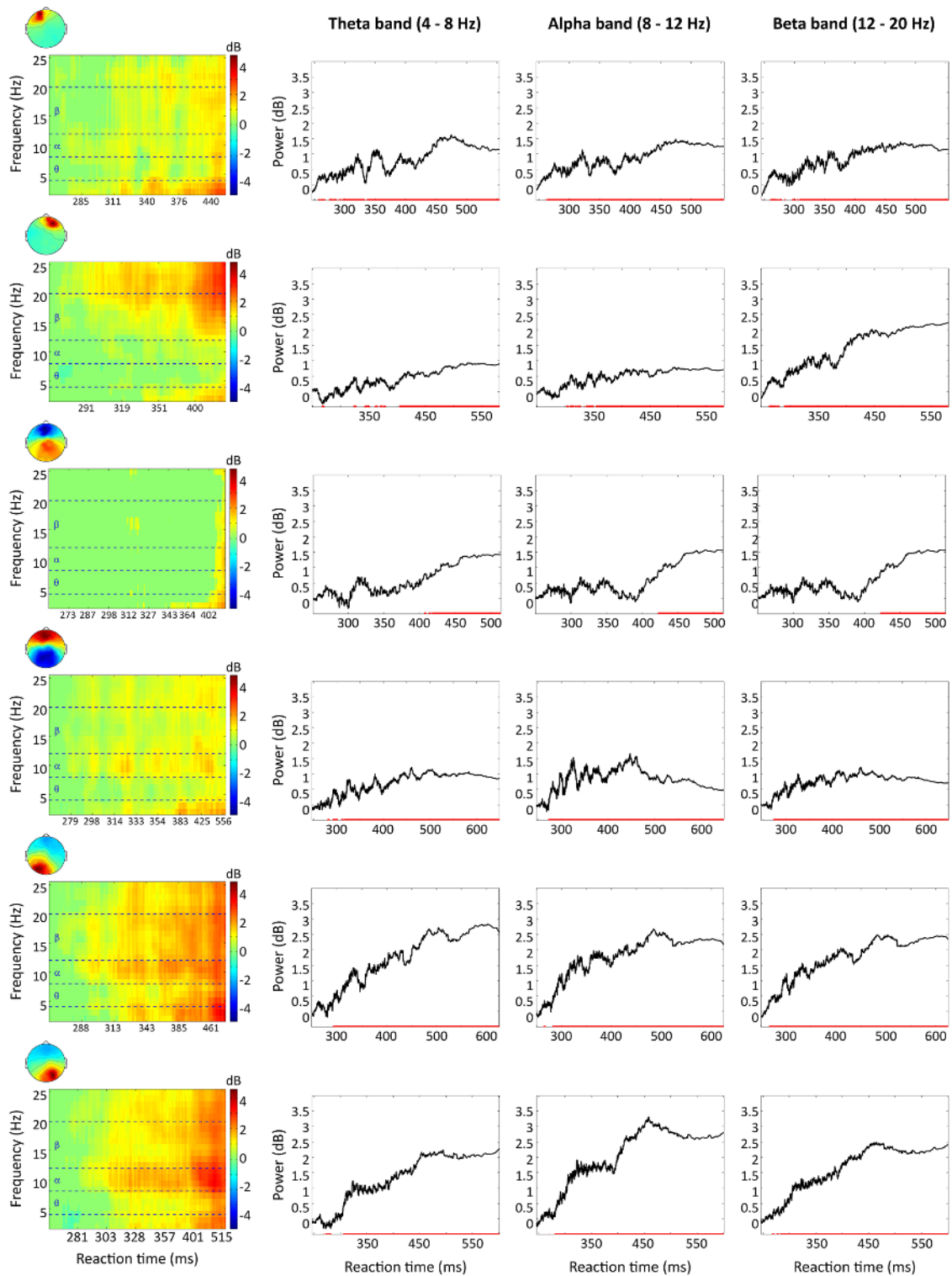


Figure 6. Tonic EEG dynamics for cluster of interest. Left image shows shifts in mean frequency power from the short-RT trials for all frequencies. The three plots to the right shows the mean power increment for theta, alpha and beta bands. Red horizontal lines represent significant changes from the power of the short-RT trials.

3.6. Discussion

This experiment addressed physiological correlates of cognitive-state changes that span from optimal to suboptimal performances in a vigilance task. More specifically, we analyzed the relationship between skin temperature and RT, and EEG power spectra and RT in non-sleep deprived subjects performing a long PVT to predict fatigue and attentional states which are prone to cause safety issues. Slowly-varying (tonic) and event-related (phasic) changes in EEG spectral dynamics were assessed by ICA, time-frequency analysis, and nonparametric permutation-based statistics, methods for modelling fluctuations in spectral dynamics of maximally independent EEG processes during continuous task performance.

3.6.1. Temperature

The results of the mixed effects models showed a positive relationship between both distal and DPG temperature measures and RT, which is consistent with other studies. For example, Romeijn et al. (2012) showed a positive relationship between DPG and RT on a vigilance task. These results are also consistent with findings that relate a decrement in the core body temperature with a low vigilance state, as indexed by several performance measures, like slow RTs or subjective alertness (Kenneth P Wright et al., 2002). This decrement in core body temperature is further considered as a mechanism to facilitate sleep onset (Kräuchi, 2007), which is achieved by means of opening skin capillaries to allow a heat flow to the outside, and results in a temperature increment in areas with a high density of capillaries, like the wrist. Therefore, an increment in distal or DPG temperatures may be related to a low vigilance state, as inferred from slow RTs in our cognitive task (PVT).

3.6.2. Phasic EEG dynamics

Our results showed a generalized theta burst after the stimulus presentation, which has been linked in several studies to monitoring of the task performance (see for example, Bastiaansen, Posthuma, Groot, & de Geus, 2002; Laukka, Järvillehto, Alexandrov, & Lindqvist, 1995). For parietal and frontal theta activity,

two different functional roles have been attributed. Parietal theta activity would be related to the early stages of visual processing (Yordanova et al., 2002) and would contribute to the early components of the ERPs (Gruber et al., 2005), whereas frontal theta activity would involve focused attention, which is increased by stimulus relevance (Deiber et al., 2007). It is also interesting to note the shorter latency of the right frontal theta ERS with respect to the premotor theta ERS, suggesting that these two different sources may also be implicated in different processes (i.e., the attentional network, and premotor processing).

Another distinct feature of the theta ERS in this study is that, unlike alpha or beta, it was observed in all clusters related to the attention network (i.e., parietal, central, premotor and right frontal). This would be in consonance with studies proposing theta to mediate in the interaction of areas spatially far from each other (e.g., von Stein & Sarnthein, 2000).

This presence of theta all over the attentional network, together with its implication in attentional processes mentioned above, suggest a key role of this frequency as a marker of performance fluctuation of the PVT, presumably mediating the communication between the areas implied in the attentional network.

Results of Experiment 1 also showed an alpha ERD following the response in the right parietal and central clusters, and around 300 ms after the response in the premotor clusters. In the right frontal cluster, there was a spindle of alpha around 100 ms after the target presentation.

Alpha desynchronization has been repeatedly reported in literature in relation to attentional processes (e.g., Pfurtscheller & Berghold, 1989; Van Winsum, Sergeant, & Geuze, 1984). Klimesch and colleagues (Klimesch, Doppelmayr, Russegger, Pachinger, & Schwaiger, 1998) showed that different alpha desynchronizations were related to increments in alertness and expectancy, and Pfurtscheller (1992) found that simultaneous alpha ERD and ERS could be found at different scalp locations, which would facilitate information processing in the areas related to the task by means of idling other areas that are not involved in the task. Thus, the alpha decrement in the premotor cluster could be related to a preparation for the next trial and to control the finger movements, as its latency corresponded to the

end of the feedback for the previous trial and the appearance of the red circle that marked the start of a new one (Pfurtscheller, Neuper, Andrew, & Edlinger, 1997; Pfurtscheller, Neuper, & Krausz, 2000).

Also interesting is the response-related alpha desynchronization in the parietal and central clusters, which was probably related to the P300 event-related potential (ERP) component. The P300 has been associated with both attention components and the alpha ERD (Käthner, Wriessnegger, Müller-Putz, Kübler, & Halder, 2014; Sergeant, Geuze, & van Winsum, 1987; Yordanova, Kolev, & Polich, 2001). Moreover, Makeig et al. (2004) found that the posterior P300 component was time-locked to the response in a go/no-go task, similarly to our results on EEG frequency dynamics. Therefore, the alpha ERD found in this experiment was probably related to the occurrence of a response-locked P300 component.

According to our results, alpha ERD in central and parietal clusters are the most promising indices of immediate performance, as they are highly linked to the RT, and alpha is highly related to attentional performance as shown above.

Finally, the beta desynchronization observed after the response in the parietal and central clusters could be related to a coherent brain state suppression due to finger movements (Makeig, 1993; Pfurtscheller, 1992).

3.6.3. Tonic EEG dynamics

A power spectrum increment with RT was observed in all frequency bands in all clusters, being more pronounced in the parietal clusters. In the premotor cluster, this increment started with RTs above 400ms. These results replicated an inverse relationship between power spectra and performance that has been consistently referenced in the literature with other vigilance tasks (Chuang et al., 2012; Huang et al., 2008; Huang et al., 2009; Valentino, Arruda, & Gold, 1993).

A generalized increment in alpha and theta power as performance declines might be explained by the reduction in synchronization-desynchronization patterns due to fatigue (Craig et al., 2012). This interpretation would be supported by neuroimaging studies that found an increased activity in default mode network related regions during mind wandering or attention lapses (Mason et al., 2007;

Weissman et al., 2006). When the brain enters the resting-state default mode, the interactions between different areas will diminish and also will the synchronization-desynchronization patterns, increasing thus the overall frequency power. The longer the brain stays in the resting-state, the higher the power and the RT.

In addition, a lower performance in the PVT might also be consequence of a decrement in visual attention, which has often been related to tonic power increases in posterior areas (Worden, Foxe, Wang, & Simpson, 2000). Possibly, these two explanations are not exclusive, both playing a role in boosting the power spectra in the brain as performance drops.

On the other hand, increments in the frontal beta band have been explained as an attempt of participants for maintaining a level of performance despite the fatigue, that is, tonic beta increments would be indicative of participants' higher cognitive effort (Craig et al., 2012; Huang et al., 2007). Further research collecting additional measures of this cognitive effort (e.g., by self-report) could test this hypothesis.

4. EXPERIMENT 2

In Experiment 2, we tried to replicate Experiment 1 using a shorter 20-min PVT, in order to later assess whether a predictive model could be built with a small set of data. Then, we investigated whether EEG data from the PVT could be transferred via a simple linear regression model to predict performance in a longer, simulated driving task.

We expected that increments in RT in the PVT would be linked to increments in frequency power in alpha and theta band in central and occipito-parietal brain areas. We also expected that a linear regression model that links alpha and theta frequency bands power and RT in the PVT, could be applied to the driving task to predict RT from the EEG registered while performing this task.

4.1. Participants

Twenty-one female subjects with normal or corrected to normal vision, from the University of Granada, participated in this experiment. The chronotype of subjects was assessed before the experiment using an online version of the Spanish

reduced version of the Morningness-Eveningness Questionnaire (rMEQ; Adan & Almirall, 1991). The inclusion criteria were subjects with intermediate-type chronotype and more than 6 hours of sleep the previous night. From the initial 21 subjects, one was excluded because the EEG recording was extremely noisy.

The age range was 18-40 years, with a mean age of 22 years-old (SD = 6). The average sleep duration was 8.1 hours (SD = 1.1). The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and was approved by the local ethics committee (nº: 17/CEIH/2015). Participants gave informed written consent before the study and they were rewarded with course credits for their participation.

4.2. Apparatus and Stimuli

The EEG setup and laboratory equipment were the same than in Experiment 1. The PVT task was also similar to that in Experiment 1, except for the duration (20 min instead of 45 min). The driving task was programmed ad-hoc using an open source driving simulator (OpenDS version 1.0; <http://opens.de>). It was run on an Intel Core i7 PC, with 16 GB of RAM and a 17" CRT screen with a 60 Hz refresh rate. The car was controlled through a Logitech Momo Racing wheel and pedals set. Auditory feedback of the engine was provided through loudspeakers.

4.3. Procedure

The experimental session was approximately 2 hours long. Firstly, subjects completed the online version of the rMEQ, and reported how many hours they had slept last night, at what time they woke up and whether they had had coffee that day and at what time. Before starting the experiment, subjects practiced for 10 minutes in the driving simulator. Then, the electrode net was placed, and they performed a 20-min PVT followed by a one hour driving task. Between the PVT and the driving task, subjects had a break of 10 minutes, while the experimenter loaded the driving task into the computer and re-adjusted the electrode net impedances.

In the driving task, subjects were asked to drive on a straight three lane road for one hour, at a constant speed and staying on the middle lane as centered as possible. At a random interval between 6 and 14 seconds, a sudden 'wind blow'

deviated the car either to the left or to the right, and subjects had to correct the direction as soon as possible, getting back to the center lane. The time elapsed between the wind blow and the beginning of the correction was recorded as the RT. The performance of subjects for both tasks was supervised by the experimenter using a second monitor and keyboard located in the adjacent room. If a subject got off the road, the experimenter, pressing one key in his keyboard, returned the car to the center lane.

4.4. Data analysis

First, we assessed the correlation between performance in both tasks (PVT and driving) by means of the RT. Second, we obtained the EEG dynamics from each task and calculate its relationship with performance. This step would allow us to replicate Experiment 1 and to obtain a physiological measure that could be compared between both tasks (i.e., the EEG frequency power). Finally, for every subject, we obtained her own generalized linear model (GLM) to predict RT from the different EEG frequency bands power in the PVT. The parameters of this model were then used to another GLM obtained from the driving task data, in which the subject's EEG frequency bands power data was the predictor to the RT. The correlation coefficient between the RT predicted by this model and the real RT obtained in the driving task was ultimately assessed.

All these steps are detailed below:

4.4.1. Correlation between PVT and driving

A first step to assess the prediction potential of the PVT was to compare the behavioral data (i.e., RT) between both tasks. Thus, RTs were firstly filtered by removing any RT below 100 ms (Basner & Dinges, 2011) and then, due to the skewed distribution of RTs, they were transformed into their inverse (i.e., $1/RT$) to obtain speed values for both, the PVT and the driving task. Finally, speed values from both tasks were compared using a Pearson's correlation test.

4.4.2. EEG and Independent Component Analyses (ICA)

EEG data analyses allowed us to evaluate the frequency power dynamics while performing the tasks and its potential as predictor of performance between them.

4.4.3. Generalized linear models

The EEG features obtained using the phasic and tonic analyses (see Methods in Experiment 1 above for details), together with the dipole information, were used to select the clusters of interest for every task. Then, every cluster from the PVT task was matched using its dipole location with a corresponding cluster from the driving task (see two leftmost columns in table 1). Finally, for every one of these pairs of clusters, we checked whether a subject was included in both clusters and, if so, we run, for that subject, the generalized linear effects models (GLM) analysis described in the next section.

4.4.4. Transferring model parameters between tasks

The GLM (Jiang, 2007) approach has been suggested to cope with problems related to non-normality of RT while avoiding the problems induced by an inverse transformation of the RTs due to “scale dependent” interactions (Lo & Andrews, 2015; Loftus, 1978). Three models using all trials from every particular subject were constructed, one for every frequency band (i.e., theta, alpha), including time-on-task to isolate its effect from the attentional fluctuations. Thus, we had frequency power and minute as fixed effects factors, and RT as the outcome variable. Significance of the model was calculated based on likelihood ratio test of the full model against the model without the effect in question. All calculations were performed in Matlab R2015b [MathWorks, Inc.; <http://www.mathworks.com>], using the generalized linear effects model class.

The dynamics of frequency power for theta, alpha and beta in each of these clusters were used as predictors of the RT using generalized linear effects models (GLM) analysis. Once we obtained the GLM coefficients for every predictor from the PVT task (i.e. $\beta_{0(PVT)}$, $\beta_{1(PVT)}$ and $\beta_{2(PVT)}$; see Equation 1, below), we applied those same coefficients to the corresponding GLM predictor in the driving task (Eq. 2), obtaining a predicted-RT distribution for every subject. Such predicted-RT distribution was then correlated with the observed-RT distribution using the Pearson’s r and p -values (corrected by means of FDR) to assess the prediction (Eq. 3).

1. **PVT Model:** $RT_{PVT} = \beta_{0(PVT)} + \beta_{1(PVT)} \text{ EEG-Power(PVT)} + \beta_{2(PVT)} \text{ Minute(PVT)}$

2. **Driving Model:** $RT_{\text{Driving_Predicted}} = \beta_0(\text{PVT}) + \beta_1(\text{PVT}) \text{ EEG-Power}(\text{Driving}) + \beta_2(\text{PVT}) \text{ Minute}(\text{Driving})$
3. **Pearson's Correlation:** $RT_{\text{Driving_Predicted}}$ against $RT_{\text{Driving_Observed}}$

4.5. Results

4.5.1. Correlation between PVT and driving

A positive significant correlation (see figure 1, left) was found between subject's mean speed in the PVT and in the driving task ($\rho = 0.72$; $p < .001$). Descriptive data for the PVT and the driving task were, respectively, $M = 3.43 \text{ s}^{-1}$; $SD = 0.44$ and $M = 2.76 \text{ s}^{-1}$; $SD = 0.26$. We also tested the agreement between these two measures using a Bland-Altman plot. Thus, figure 7 (right) show that all observations are within the 1.96SD limits of agreement. There is also a bias of -0.7243 ms , indicating a higher speed of response in the PVT vs the driving task, something clearly expected due to the different ways of response in both tasks (i.e., just a keystroke in the PVT vs a steering-wheel correction in the driving task).

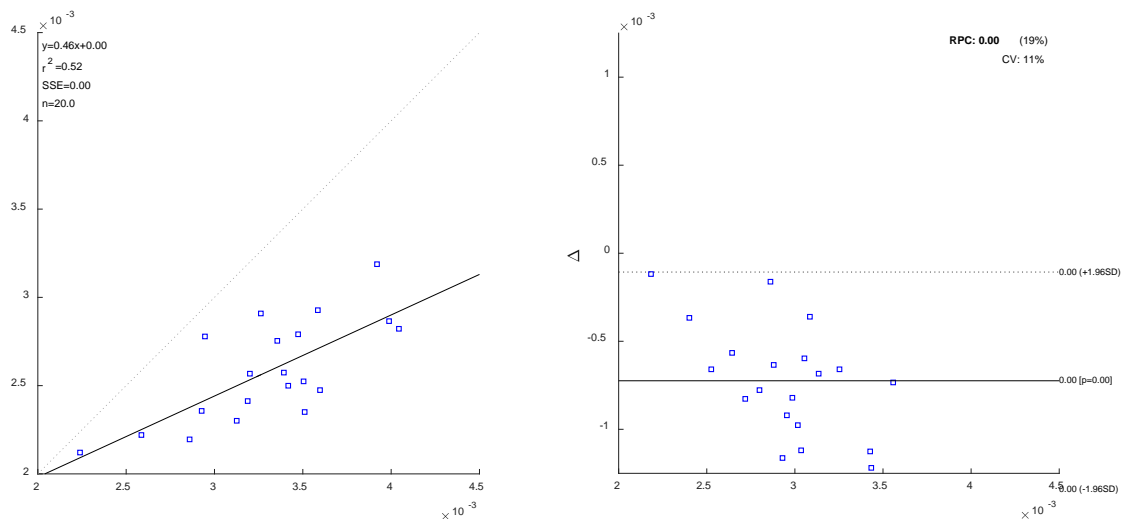


Figure 7. Pearson correlation between subjects mean speed (1000/RT) in the PVT and in the driving task (left) and Bland-Altman plot for the relationship of the

difference between RT in the PVT and in the driving versus their average values (right).

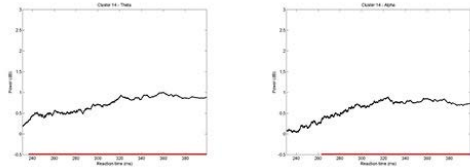
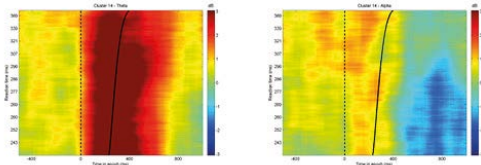
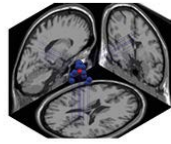
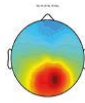
4.5.2. Phasic and tonic EEG

A total of 19 clusters for the PVT and 17 for the driving task were obtained after the clustering process. After excluding clusters related to muscle noise and eye blinks, a first subset of clusters was obtained based on their scalp maps and dipole location, from which 8 clusters from the PVT and 9 clusters from the driving task were selected. The scalp maps, dipoles and phasic and tonic analyses for these clusters are represented in figure 8.

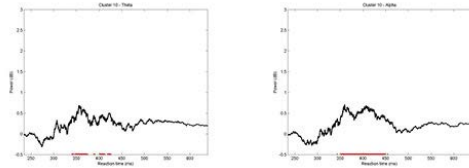
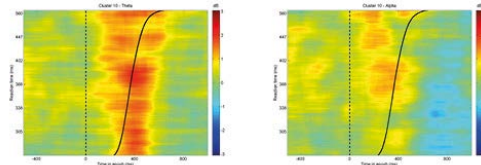
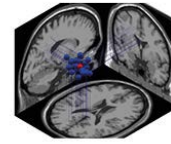
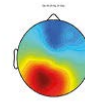
Three clusters from the PVT (14, 16 and 17) and five clusters from the driving task (10-13, 16-5 and 4) were located in brain areas related to the fronto-parietal attentional network and the default mode network. Moreover, the dipole locations of these clusters and the event related synchronization (ERS) and desynchronization (ERD) patterns exhibited in the phasic analyses are similar to those found in Experiment 1. For instance, we can see for the alpha band (see Phasic Analyses section in figure 5) a statistically significant increment of power just before the response and an abrupt ERD after the response.

The tonic analyses also replicated the results found in Experiment 1, showing an increment in tonic power as performance decreased (see figures 6 and 8). This increment happened for the alpha and theta bands in both, PVT and driving task clusters, except for the clusters located on the cingulate anterior area, for which the statistically significant increment only occurred for the PVT task.

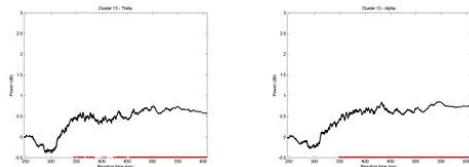
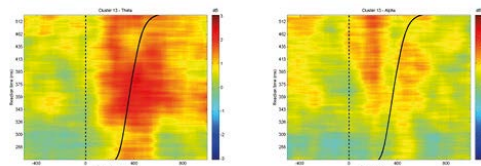
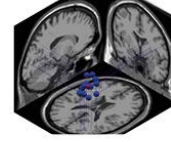
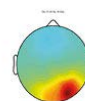
14



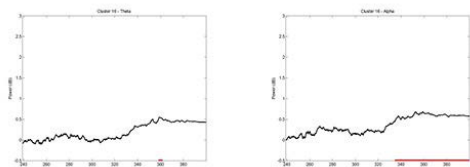
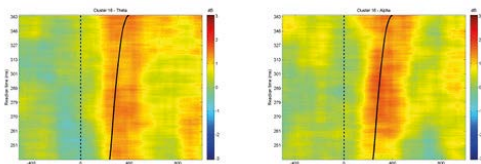
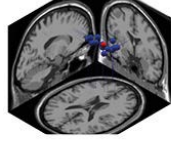
10



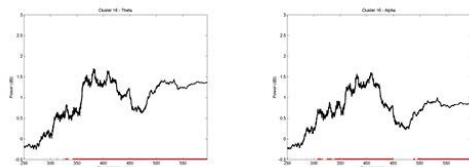
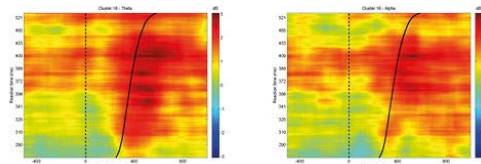
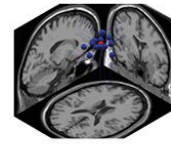
13



16



16



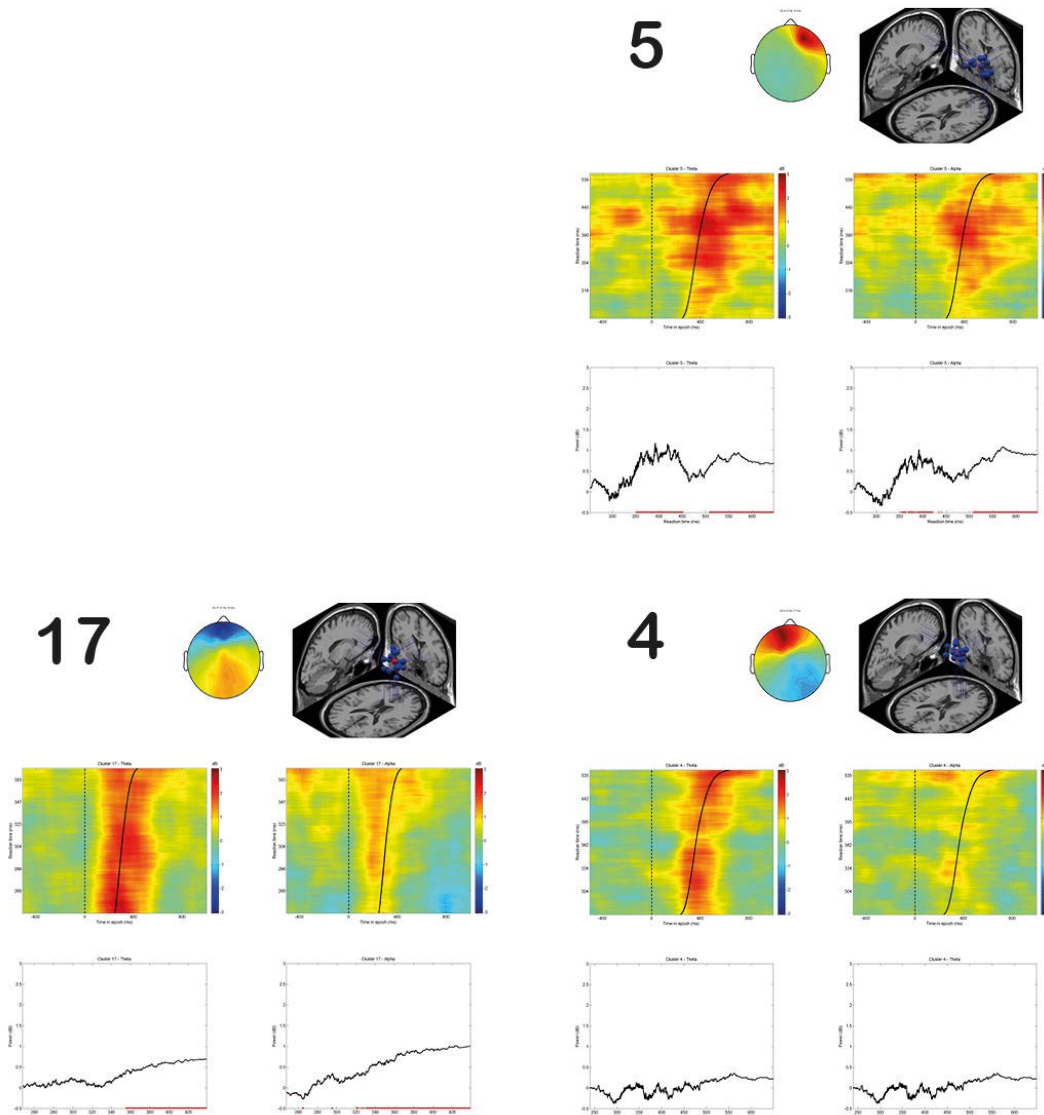


Figure 8. Scalp maps, dipole locations and phasic and tonic analyses for the PVT (left) and the driving task (right).

4.5.3. Generalized linear models

The GLM analyses results showed variable results across subjects, with a positive and statistically significant correlation between predicted-RTs and observed-RTs for some subjects, and no correlation at all or even a negative correlation for other subjects (see table 1).

More specifically, subjects 5, 8, 9, 14 and 16 present a positive significant correlation for both alpha and theta frequency bands, while subjects 2, 17 and 18

present this positive correlation only for either alpha (subjects 2 and 18), or theta (subject 17) frequency band, being the correlation non-significant for the other band.

Subjects 1, 4 and 13 present a negative significant correlation in alpha and theta, and subject 19 only present this negative correlation in the alpha band.

Subjects 5, 6, 7, 10, 12 and 15 do not show any significant correlation in either frequency band. While subject 3 present a positive correlation in alpha and theta in three pairs of clusters, and a positive correlation for theta and a negative correlation for alpha in one pair of clusters.

Finally, subject 11 is not represented in any clusters, and therefore, a GLM analysis for this subject was not performed.









Cluster PVT	Cluster Driving	Brain area	Subject	Theta (r, p value)		Alpha (r, p value)	
14	10, 13	Right parietal – Precuneus (BA 31)	1	-0.346	0.009	0.132	0.332
			3	0.679	0.000	0.687	0.000
			5	0.191	0.141	0.190	0.147
			8	0.443	0.000	0.398	0.001
			9	0.383	0.002	0.409	0.001
			10	-0.098	0.459	-0.103	0.439
			13	-0.698	0.000	-0.662	0.000
			15	-0.202	0.121	-0.020	0.878
			16	0.308	0.014	0.318	0.011
							
16	16, 5	Middle Frontal gyrus (BA 10)	3	0.601	0.000	0.652	0.000
			7	0.176	0.180	0.105	0.541
			12	-0.162	0.197	-0.157	0.212
			13	-0.679	0.000	-0.658	0.000
			19	-0.191	0.145	-0.318	0.019
			20	-0.387	0.002	-0.414	0.001
			4	-0.559	0.000	-0.521	0.000
							
17	4	Right limbic lobe – Cingulate anterior (BA 24)	5	0.212	0.101	0.209	0.106
			6	0.154	0.236	-0.125	0.337
			7	-0.110	0.403	-0.106	0.421
			9	0.274	0.033	0.350	0.006
			10	-0.117	0.377	-0.090	0.499
			14	0.341	0.006	0.379	0.002
			16	0.287	0.022	0.292	0.019
			18	0.088	0.505	0.238	0.070
							

Table 1. Pearson correlation between RT predicted and observed in the driving task. First and second columns represent the clusters compared and used to obtain the EEG data. Third column indicates the dipole location by means of its Talairach coordinates and the Brodmann area which contains them. Fourth column are the subjects included in both clusters. Last two columns indicate the correlation coefficient and its significance.

4.6. Discussion

In Experiment 2, we replicated results from Experiment 1 (i.e., that pre-target power increments in the theta and alpha frequency bands are related to slower RTs) in a 20-min PVT and also in a simulated driving task. The sources of this EEG activity were also similar to those of Experiment 1, being located in brain areas related to the fronto-parietal attentional network, like the middle frontal gyrus and the cingulate cortex, as well as in the precuneus, a structure related to the default mode network.

We have, likewise, established a link between the behavioral and cognitive processes related to performance in a simple task, like the PVT, and a complex task, like driving. This result is important because it implies that any performance predictor obtained from the brain processes during the PVT could be potentially applied to the driving task. Finally, we have tested one such index (the EEG frequency power), and assessed to what extent the underlying EEG dynamics related to the performance of a 20-min long PVT can be transferred to a driving task.

4.6.1. Psychomotor Vigilance Task

Three components from the 20-min PVT presented a tonic power increment in alpha and theta frequency bands related to performance decrements (i.e., slower RTs). These components were located in the precuneus, the cingulate cortex and the middle frontal gyrus, areas that have been linked to performance in other attentional tasks by means of increments in alpha and theta frequency power (Craig et al., 2012; Martel et al., 2014; Shou & Ding, 2013).

Although the EEG dynamics from these three components replicated those from Experiment 1, the 45-min PVT presented clearer EEG patterns in both hemispheres. Also, a shorter PVT reduce the data available for the ICA algorithm, resulting in a worse solution for every component (Onton, Westerfield, Townsend, & Makeig, 2006).

The alpha and theta frequency dynamics of these components, together with their locations, suggest a role in the attentional processes related to the performance

fluctuations in *the* PVT, as we have discussed in Experiment 1, and therefore, they can be used to build and test a predictive model of RTs in the PVT.

4.6.2. Driving task

Simulated driving is a more complex task than the PVT. Even a simplified driving task, as the one used here, implies higher motor demands, spatial orientation and sensory integration, apart from selective and sustained attention (Lal & Craig, 2001). Nonetheless, the components locations and frequency dynamics matched those observed in the PVT, suggesting that they reflect similar processes in both tasks. Thus, five components located on the precuneus, the parietal cortex, the middle frontal gyrus and the cingulate cortex exhibit tonic power increments in alpha and theta frequency bands preceding slower RTs. This result is important as it suggests that any index that evaluates these processes in one task could be, potentially, directly applied to the other task.

Moreover, the frequency dynamics and brain areas found in the driving task are in consonance with previous literature on driving performance prediction (C.-H. Chuang et al., 2014; R.-S. Huang et al., 2009; C.-T. Lin et al., 2010). Therefore, we can conclude that the neural basis related to these results are linked to the attentional state of subjects, and that these brain processes affect in a foreseeable way to their performance in the driving task.

Apart from the consistent EEG frequency patterns obtained through both PVTs (i.e., 45-min PVT and 20-min PVT), and the driving task, which are related to performance in these tasks, results showed a high intra-subject correlation in performance (measured as the response speed) between the driving task and the 20-min PVT, which indicates that subjects who performed faster in the PVT (i.e., better attentional state), also performed faster in the subsequent driving task. This is a very interesting result, as it implies that we can build a distribution of PVT performances for every subject and obtain a ranking of good and bad global attentional states, and then extrapolate this result to predict how he/she could perform in a driving session. Nonetheless, the behavioral data alone can only be used as a general index, but not as a continuous measure of fatigue, given that, as (Baulk et al., 2008) showed, the impairment obtained in a series of repeated measures would be more noticeable in the driving task than in the PVT, resulting

in a spurious correlation between these two measures. Moreover, given that the attentional state of the subjects is not constant, we cannot predict if a performance decline would happen some minutes after the driving session started, even if the PVT data indicated an optimal attentional state just before driving. Therefore, this index would only be useful to prevent short-term low attentional states.

Summarizing, we have found similar frequency dynamics in the PVT and the driving task (i.e., a tonic increment with RT in theta and alpha bands), which have been associated with attention-related performance in these tasks, and they are located in the same brain areas, linked to sustained attention and fatigue. The implications of this result are crucial for this research, as we have found a common predictor of performance in the PVT and the driving task, which can be potentially transferred between those tasks by means of a predictive model.

4.6.3. Regression model

Using linear regression as a predictive model has two main advantages over other models. First, machine learning algorithms need to be trained with a huge amount of data (Liu et al., 2016; Vuckovic, Radivojevic, Chen, & Popovic, 2002; Wang, Sun, Fang, Fu, & Stipancic, 2017), while in a regression model only require adjusting a few parameters, usually one for each predictor. Second, unlike a simple behavioral correlation between tasks, a regression model can predict performance ups and downs (i.e., changes in RT) in very short time scales, and can predict performance seconds in advance.

Here, to assess to what extent the underlying EEG dynamics related to the performance of a 20-min long PVT could be transferred to the driving task, we had to test whether the model obtained using the PVT EEG data was able to predict RTs in the driving task. Following a similar approach to the one used by Touryan et al. (2014), we fitted a linear regression model using a simplest task (i.e., the PVT), and applied to the complex task (i.e., the simulated driving). However, unlike the study by Touryan et al. (2014), the model was constructed using only 20 min of data, instead of 60 minutes, which resulted in less data available for the model. Also, a shorter task can reduce the sensitivity of a performance task (Mullaney, Kripke, Fleck, & Johnson, 1983).

Nonetheless, our results showed that using a simple regression model (GLM), accurate predictions can be achieved in a few subjects ($n = 8$). The question is why this model did not work for all subjects. Two possible explanations are considered: 1) There are different brain processes involved in these tasks, and 2) the tasks share similar brain processes, but the indices obtained through the analysis of the EEG frequency power are task-specific and, therefore, cannot be transferred between tasks. The latter is easily rejected given that, if indices were task-specific, they would not have worked for any subject. It can be argued, nonetheless, that processes are different, but subjects use a similar strategy in both tasks. However, if this were the case, it would make no difference, given that the model would still be able to predict performance in both tasks.

Regarding the first explanation (i.e., that there are different processes involved in these tasks), we have shown that alpha and theta frequency bands dynamics are related to performance changes in both, the PVT and the driving task, as explained above. These findings suggest that the underlying attentional processes grasped by the EEG frequency analyses are similar in both tasks, or at least, there is a subset of processes that overlap in both tasks. Therefore, a common performance model can be obtained from one task and applied to the other task, although the complexity of such a model could be a prime factor regarding its generality. In other words, some individual-specific factors which are not included can result in an incomplete model. Also, inter-individual differences in driving ability, and systematic differences in the impact of fatigue (e.g., Van Dongen, Baynard, Maislin, & Dinges, 2004), could play a substantial role in this case. These factors not only can affect differently to the subjects, but also, its effect on the model can be more evident as the task increments its duration.

5. LIMITATIONS OF THE STUDY

Our sample for both experiments included only women, but although gender differences have been assessed in vigilance tasks (Waag, Halcomb, & Tyler, 1973), it seems that these differences are not influenced by the drowsy state of the subjects, but rather by the difference in strategy between men and women (i.e., women tend to be more accurate, while men tend to be fast, see Blatter et al.,

2006). Thus, it is unlikely that a mixed sex population would have changed the results of this study in a significant way.

Regarding Experiment 1, a more evident concern arises when registering temperature from an only female sample with no control of the menstrual cycle. Nonetheless, Shechter, Boudreau, Varin, & Boivin (2011) found no difference in maximum, minimum, circadian amplitude nor interaction between distal temperature and distal to core gradient temperature with menstrual phase. Other studies have found that circadian phase of both the core body temperature (Baker, Driver, Paiker, Rogers, & Mitchell, 2002; Shibui et al., 2000; Wright & Badia, 1999) and the distal temperature (Shechter et al., 2011) is not altered by menstrual phase. Finally, although severe premenstrual syndrome (PMS) might also affect the EEG and PVT results (Baker & Colrain, 2010), other studies have found no effect of PMS in sustained attention (Jensen, 1982; Keenan, Lindamer, & Jong, 1995; Morgan & Rapkin, 2012).

6. CONCLUSIONS AND FUTURE RESEARCH

Nowadays the need for providing services day and night has been increased due to the demands of a 24/7 society, resulting in more than 20% of the population working outside the regular working day hours (Rajaratnam & Arendt, 2001). Shift workers, all night long bus and truck routes, air traffic control, are a few examples of tasks requiring good capabilities for sustaining vigilance and in which fatigue can be a key safety issue. Thus, finding indices to predict attentional fluctuations that can prevent accidents is an important research aim.

In this study, we aimed to predict attentional fluctuations in a common, every day task, such as driving, by means of data obtained using a simple short RT task, such as the PVT. In Experiment 1 we show for the first time that the EEG frequency dynamics are related to the PVT performance. Then, in Experiment 2, we assessed whether the EEG data from a short PVT could be used to predict performance in a long simulated driving task. Thus, although the final aim of the study was not met (i.e., to obtain a model that could predict performance in the driving task), most of our other hypotheses in this study have been confirmed. Thus, in Experiment 1, we observed a relationship between theta and alpha bands frequency power and

performance in the PVT; we likewise obtained a minute-by-minute correlation between RT and skin temperature. In Experiment 2 we confirmed that the PVT, even a short 20-min version, is a good tool to grasp attentional fluctuations in non-deprived subjects; and, second, that the driving task share some attentional related processes with the PVT and these processes can be modelled (at least in some subjects) by means of the EEG frequency dynamics. Therefore, the potentiality of the PVT as a vigilance performance predictor is promising, and for future research we need to know more about how the EEG correlates of attention in this task are affected by subject-specific factors that could lead to find a suitable model that can be applied to every subject.

Discusión General

1. Consideraciones previas

Hoy día la preocupación de los fabricantes de vehículos por la seguridad no para de crecer, lo que se refleja en una gran inversión en investigación destinada a prevenir accidentes. Gran parte de esa prevención se basa en poder identificar estados de baja atención en los conductores, ya sea por fatiga o por distracción, que pueden resultar en accidentes. El objetivo principal de esta tesis ha sido contribuir a esta investigación, identificando índices fisiológicos relacionados con las fluctuaciones de atención y evaluando su capacidad predictiva durante la conducción. Para ello nos hemos basado en una tarea sencilla de tiempo de reacción, como es la PVT, para crear un modelo individualizado que nos permita predecir lapsos atencionales en tareas más complejas, como la conducción.

2. Resumen general de los resultados

Experimento	Objetivo principal	Diseño experimental	VVII	VVDD	Resultados principales
1	Analizar efecto de factores circadianos en la conducción	13 participantes matutinos y 12 vespertinos ; 2 sesiones de PVT + conducción, a las 8:00h. y a las 20:00h.	Cronotipo (Mat, vesp), hora del día (8 am; 8pm; intrasujeto)	Subjetivas (rmeq; cuestionarios de activación y afecto) RT para la PVT EEG y error de posición para la conducción	Efecto de hora del día para los vespertinos en la conducción (mayor decremento de vigilancia por la mañana)

					Incremento generalizado de la potencia de alfa con el tiempo en tarea para ambos cronotipos
2	Estudiar las dinámicas del EEG y la temperatura durante la realización de la PVT	17 participantes de cronotipo intermedio realizaron una PVT de 45 minutos		RT EEG (análisis de frecuencias usando ICA y localización de fuentes) y temperatura de la piel (distal, proximal y DPG)	Incremento de potencia en theta, alfa y beta al aumentar los RTs. Incremento de temperatura distal y DPG junto a un incremento de los RTs.
3	Transferir un modelo predictor de fatiga entre la PVT y una tarea de conducción	21 participantes de cronotipo intermedio realizaron una PVT de 20 minutos y una tarea		EEG (análisis de frecuencias usando ICA y localización de fuentes) para la PVT y para la	El modelo de regresión fue positivo para 2 sujetos en alfa, para 1 sujeto en theta, y

		de conducción de 60 minutos. Un modelo de regresión ajustado para la PVT se usó para predecir la ejecución en la conducción.		tarea de conducción RT para la PVT y para la tarea de conducción.	para 5 sujetos tanto en alfa como en theta. Para 13 sujetos restantes la predicción no funcionó.
--	--	--	--	---	---

El Experimento 1 simulaba una situación cotidiana, es decir, la conducción por autopistas monótonas y sin tráfico por la noche o por la mañana temprano, y abordó cómo la duración de la conducción, la hora del día, y las diferencias individuales en cronotipo (por primera vez en la literatura) influían en la ejecución y se reflejaban en índices fisiológicos como la temperatura y el EEG. Los resultados mostraron que el decremento de vigilancia en la conducción (mayor error de posición con el tiempo en tarea) era sensible a factores circadianos, es decir, estaba modulado por la hora del día en que se realizara la tarea, aunque solamente para los sujetos de cronotipo vespertino, quienes podían minimizar la aparición del decremento de vigilancia al realizar la tarea en su hora óptima del día (i.e., a las 20:00 horas). Además, observamos que el decremento de vigilancia se reflejaba en el EEG con un aumento de potencia en la banda de frecuencia alfa, aunque este efecto no se veía afectado por factores circadianos.

En el Experimento 2 nos centramos en la respuesta de dos marcadores psicofisiológicos (el EEG y la temperatura) ante las fluctuaciones de atención producidas por la realización prolongada de una tarea de vigilancia (la PVT), eliminando la influencia de los factores circadianos (todos los sujetos tenían

cronotipo intermedio y las tareas se realizaron a horas de día no extremas). Los resultados de este estudio revelaron una relación directa entre la ejecución en la PVT y la dinámica del EEG, mostrando que la potencia en tres bandas de frecuencia (theta, alfa y beta) podía predecir el tiempo de respuesta en la tarea (i.e., los tiempos de respuesta más lentos iban precedidos de una mayor potencia en estas bandas de frecuencia). Además, mediante el análisis de componentes independientes (ICA) y localización de fuentes se comprobó que estas fluctuaciones se produjeron en zonas centrales y fronto-parietales, relacionadas con la red por defecto y la red atencional fronto-parietal. Por último, los resultados también mostraron una relación entre ejecución y temperatura. Más concretamente, un análisis de regresión mostró que incrementos en la temperatura distal o en el gradiente entre la temperatura distal y proximal podían predecir incrementos en los tiempos de reacción. Más concretamente, el análisis de modelos mixtos indicó que incrementos de un grado de temperatura suponían incrementos de 10 y de 8 ms en el tiempo de respuesta para la temperatura distal y para el gradiente, respectivamente.

El Experimento 3 planteaba dos hipótesis. Primera, que los resultados obtenidos en el estudio previo podrían ser replicados en una tarea más compleja como es la conducción simulada. Y segunda, que los cambios de frecuencia del EEG, que predecían los tiempos de reacción de la PVT, podría transformarse en un índice que predijera el tiempo de respuesta en la tarea de conducción. Los resultados confirmaron la primera hipótesis, mostrando que la dinámica del EEG en la conducción replicaban los obtenidos en el estudio previo, esto es, que un incremento de la potencia en las principales bandas de frecuencia precedía a una peor ejecución (peores tiempos de reacción) en la tarea de conducción. La segunda hipótesis se puso a prueba mediante un modelo de regresión lineal. Los resultados indicaron que, a pesar de ser un modelo sencillo en el que minimizábamos el uso de variables específicas de los sujetos, éste era capaz de predecir, para un número limitado (8 sujetos de 21) de sujetos, la ejecución en la tarea de conducción, a partir de la dinámica del EEG en esta tarea y los parámetros obtenidos para cada sujeto en la PVT.

3. Ritmos circadianos

Aunque el efecto de la hora del día sobre la conducción había sido estudiado con anterioridad (M G Lenné, Triggs, & Redman, 1997), y también se conocía el efecto del cronotipo sobre el rendimiento cognitivo en una gran variedad de tareas (Hasher, Chung, May, & Foong, 2002; Hornik & Miniero, 2009; Rowe, Hasher, & Turcotte, 2009; Yang, Hasher, & Wilson, 2007), sorprendentemente no se había estudiado la interacción de estos factores circadianos y su efecto en la conducción.

Nuestros resultados mostraron por primera vez que el decremento de vigilancia en una tarea de conducción podía modularse por la interacción entre cronotipo y hora del día. Esta interacción, que fue muy clara para el grupo de vespertinos, no apareció, sin embargo, en el grupo de matutinos, que mostraron una ejecución similar en ambas sesiones, es decir, independientemente de la hora del día. Este es un resultado que no concuerda con nuestra hipótesis inicial, en la que esperábamos la aparición del efecto de sincronía (C. P. May & Hasher, 1998), es decir, que ambos grupos de cronotipos mostrarían un decremento de vigilancia más acusado en la sesión correspondiente a su hora mala del día.

Una posible explicación de este resultado sería la baja demanda cognitiva de la tarea. Monk & Leng (1986) sugerían que tareas que implicaran una alta carga de recursos cognitivos serían mejores diferenciando cronotipos. Sin embargo, de ser así, los vespertinos tampoco deberían haber mostrado el decremento de vigilancia por la mañana, sobre todo teniendo en cuenta que no había privación de sueño para este grupo (i.e., no hubo diferencias en las horas de sueño de la noche previa al experimento).

También es posible que el grupo de matutinos consiguiese mitigar el decremento de vigilancia en la sesión de tarde sacrificando la rapidez de respuesta a cambio de una mayor precisión, como ha sido reportado en Reinke, Özbay, Dieperink, & Tulleken (2015). Esta estrategia sería especialmente útil en una tarea como la nuestra, donde no se mide el tiempo de reacción, sino la precisión en mantener el coche en el centro de la carretera. Esta explicación también encajaría en los estudios que sostienen que los matutinos poseen un mejor mecanismo de compensación de fatiga (Martin, Hébert, Ledoux, Gaudreault, & Laberge, 2012).

Por último, debemos considerar la posibilidad de que la sesión de la tarde no se realizara a una hora tan disruptiva para los matutinos como la sesión de la mañana para los vespertinos, ya que se realizó durante las horas de la “zona prohibida para dormir” (entre las 8 y las 10pm), cuando el nivel de alerta es particularmente alto (Lavie, 1986) e incluso puede producirse una mejora en la ejecución de tareas de vigilancia (Shekleton et al., 2013).

4. La temperatura como predictor de la atención

La temperatura de la piel es una medida interesante desde el punto de vista de la ergonomía: fácil de registrar, barata y no invasiva, lo que la convierte potencialmente en un excelente índice de fatiga en tareas de conducción. Nuestros resultados muestran una relación directa entre las variaciones de temperatura y los tiempos de reacción en la PVT, es decir, que un aumento de los tiempos de reacción va acompañado de un aumento de la temperatura distal o del gradiente de temperatura. Este resultado es muy interesante ya que muestra una relación directa entre la temperatura y la ejecución en la PVT, una relación que está en consonancia con la literatura previa sobre temperatura y vigilancia (Romeijn, Raymann, et al., 2012).

Por otro lado, la temperatura proximal no mostró una relación significativa con la ejecución, en contra de lo esperado. Otros estudios (Tania Lara et al., 2018; Romeijn & Van Someren, 2011) han encontrado que incrementos en la temperatura proximal están relacionados con incrementos en los tiempos de reacción, aunque en el caso de Lara et al. (2018), esta relación también resultó no significativa en uno de los experimentos. Además, la temperatura proximal se ha descrito como un indicador de la temperatura central del cuerpo, cuyos incrementos se asocian a estados de baja somnolencia (Van Someren, 2006). Estos datos, por lo tanto, serían contrarios a la relación entre temperatura proximal y ejecución en tareas de vigilancia que se describe en los estudios anteriores.

Otra perspectiva la aportan estudios que ven a la temperatura no como un indicador, sino como un regulador de la vigilancia. Estos estudios han mostrado que manipulando la temperatura corporal se puede afectar la ejecución en tareas

de vigilancia (Raymann & Van Someren, 2007). Desde este punto de vista, la temperatura debería ser considerada más una causa que un efecto de las fluctuaciones de atención. En cualquier caso, el lento curso temporal de las variaciones en temperatura (del orden de minutos), hacen complicado discernir en nuestros resultados si la temperatura es causa o efecto de los tiempos de reacción. Para discernir el papel de la temperatura, sería interesante, en una investigación futura, medir este efecto de manipulación de la temperatura en tareas de vigilancia mediante el análisis de frecuencias del EEG.

La temperatura de la piel, pues, puede ser una variable muy valiosa en la prevención de accidentes, bien a través de su manipulación para mejorar la ejecución, o bien como indicador para prevenir estados de somnolencia inminentes. Así, usada en conjunción con el EEG se puede obtener un índice de atención más completo, en el que el sistema puede detectar momentos globales de baja capacidad atencional gracias a la temperatura, al mismo tiempo que tenemos un índice inmediato, el EEG, que puede predecir estas fluctuaciones atencionales en el rango de milisegundos gracias a su gran resolución temporal.

5. El EEG como predictor de la atención en la PVT y la conducción

Los resultados obtenidos al realizar el análisis de frecuencias del EEG apoyan nuestra hipótesis de que la dinámica de potencia en las bandas theta y alfa pueden predecir las fluctuaciones de atención en tareas de vigilancia. En los experimentos 2 y 3 de esta tesis, las aportaciones principales son las siguientes: Primero, realizamos, por primera vez en este tema de investigación, un análisis de la dinámica de potencia del EEG durante la realización de una PVT, poniendo en relación las fluctuaciones en las principales bandas de frecuencia con los tiempos de reacción en la tarea. Segundo, replicamos este resultado en el Experimento 3 para una PVT más corta y, más importante aún, para una tarea de conducción simulada. Y, por último, el uso del Análisis de Componentes Independientes (ICA) en ambos experimentos nos permite obtener información acerca del área cerebral donde se originan estas fluctuaciones.

Estudios previos han mostrado que theta presenta el comportamiento más consistente en los experimentos donde se usan tareas de conducción simulada, mostrando un incremento de potencia asociado a un descenso de la ejecución. Alfa también es un indicador comúnmente usado en estas tareas y, en general, muestra el mismo comportamiento que theta, aunque otros estudios encuentran una relación inversa entre alfa y la ejecución o ninguna relación en absoluto. Para explicar esta discrepancia se ha hecho referencia a la sensibilidad de alfa al estímulo o los eventos del experimento, lo que enmascararía su relación con la ejecución (ver la revisión de Lin et al., 2012).

Es importante recalcar que nuestros resultados han sido constantes a lo largo de todos los experimentos y en todas las tareas usadas (dos tareas diferentes de simulación de conducción y dos PVT de 20 y 45 minutos de duración), aunque si bien en el Experimento 1 sólo pudimos constatar un incremento global de la potencia del EEG con el paso del tiempo, en los dos siguientes estudios, gracias al uso de técnicas como el análisis independiente de componentes y la localización de dipolos, pudimos asociar esos incrementos en potencia con la ejecución en las tareas, independientemente del deterioro producido por el paso del tiempo. Este último resultado es muy importante, porque significa que es posible predecir lapsos puntuales de atención, aunque la ejecución global del sujeto sea buena. Estos lapsos estarían relacionados con pequeñas distracciones más que con un estado de somnolencia.

En nuestros estudios, las fluctuaciones de la potencia del EEG antes del estímulo, localizadas por medio de sus dipolos, se originaban en zonas cerebrales localizadas en la red atencional fronto-parietal y la red por defecto. Una mayor activación en la red por defecto se ha relacionado con una peor ejecución en la PVT (Drummond et al., 2005; Zhu et al., 2018) y otras tareas atencionales (Eichele et al., 2008). Sin embargo, nuestros resultados muestran que una peor ejecución va acompañada de un incremento de alfa en esta zona. Este resultado parece contradictorio, ya que alfa se considera un mecanismo inhibitorio (Berger, 1929), por lo que un aumento de este ritmo en la red por defecto implicaría una disminución de su actividad y, por lo tanto, una menor distracción de la tarea principal. De hecho, esta perspectiva donde la red atencional y la red por defecto actúan de forma opuesta

es común en la literatura (Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003b; Weissman et al., 2006). Sin embargo, (Bekhtereva et al., 2014) también observó una mayor actividad de la red ejecutiva durante episodios de desenganche de la tarea (i.e., *mind wandering*), de forma que es compatible una desactivación global de ambas redes (la red atencional y la red por defecto) en situaciones de poca atención a la tarea.

Respecto a la dinámica física del EEG, uno de los resultados más interesantes es la supresión de alfa justo tras la respuesta en áreas localizadas en la red por defecto (i.e., el precuneus) y áreas posteriores de la red atencional. Esta supresión se da en ambas tareas, tanto en la PVT como en la tarea de conducción simulada, y sugiere que, mientras no es necesario realizar ninguna acción en la tarea, los recursos se dirigen hacia la red por defecto, lo cual viene indicado por un aumento generalizado de alfa, pero en el momento en que la tarea exige una respuesta, se produce una inhibición física de alfa para volver a engancharse atencionalmente en la tarea. Este “enganche” se iría haciendo cada vez más difícil con el paso del tiempo, produciendo el decremento de vigilancia. Estos datos, pues, apoyarían el modelo del control de recursos (Thomson et al., 2015) para explicar los lapsos y el decremento de vigilancia.

Por último, una de las implicaciones más interesante de nuestros resultados es la que surge de la replicación de dinámicas espectrales y localización de dipolos en ambos experimentos y en las tres tareas. Esta constancia de resultados sugiere que los procesos subyacentes a las fluctuaciones atencionales, o al menos una parte de ellos, son similares y, por lo tanto, potencialmente generalizables entre una tarea sencilla de tiempo de reacción como es una PVT de 20 minutos, y otra tarea más larga y compleja, como una tarea de conducción simulada de 60 minutos de duración, aunque en esta última tarea también tengan relevancia otros procesos como la coordinación viso-espacial o de tracking.

6. Transferencia entre PVT y conducción

El último objetivo de esta tesis era conseguir predicciones del estado atencional de los conductores usando la dinámica de su EEG. Para ello, construimos un modelo

predictivo basado en modelos de regresión lineal, que fue ajustado individualmente usando datos específicos de cada sujeto obtenidos mientras realizaban una PVT de 20 minutos.

Este modelo y los resultados obtenidos son similares a un estudio previo realizado por Touryan et al. (2014), aunque nuestro estudio tiene dos diferencias metodológicas importantes. En primer lugar, el uso de la PVT en lugar de una tarea RSVP. La RSVP puede mostrar efectos de práctica y es menos sensible a los efectos del decremento de vigilancia que la PVT (Bekhtereva et al., 2014). En segundo lugar, a diferencia del estudio de Touryan et al. (2014), nosotros usamos ICA para obtener componentes independientes con la intención de aislar mejor los distintos procesos subyacentes en nuestro modelo. Sin embargo, es interesante que, en ambos estudios, el modelo funcionó para aproximadamente un tercio de los sujetos de una muestra similar. Una posible explicación de por qué nuestro modelo no funcionó en muchos sujetos, es que las dos tareas del experimento (la PVT y la conducción simulada) son muy diferentes. Touryan, Lance, Kerick, Ries, & McDowell (2016) sugieren que, debido a estas diferencias, un modelo basado en EEG resultaría incompleto ya que algunos procesos no estarían ocurriendo en ambas tareas. Sin embargo, esto no explicaría por qué funciona en algunos sujetos.

Otra posible explicación se pueda obtener desde el punto de vista del modelo del control de recursos (Thomson et al., 2015), que supone una competición constante por los recursos disponibles entre las áreas destinadas a la ejecución de la tarea y las áreas de la red por defecto. Según esta perspectiva, un modelo predictivo debería tener en cuenta las interacciones entre la actividad de zonas situadas en ambas áreas, y no de estas áreas por separado, como hace nuestro modelo. Si esta interacción es más fuerte en algunos sujetos que en otros (o entre una y otra tarea), esto podría explicar por qué el modelo actuó de forma diferente para ellos. Este sería un punto interesante para analizar en un estudio futuro.

La predicción de lapsos en la conducción es un tema de mucho interés actualmente, y no es extraño encontrar estudios que, usando técnicas de aprendizaje automático, utilizan los datos del EEG para predecir la ejecución en la conducción. Por ejemplo, usando máquinas de vectores de soporte (SVM) se han conseguido tasas de acierto del 97% (Ebrahimi, Mikaeili, Estrada, & Nazeran,

2008). Sin embargo, conseguir una tasa de acierto tan alta requiere aumentar considerablemente la complejidad del modelo, así como una gran cantidad de datos para entrenarlo.

Nosotros hemos desarrollado un modelo predictor simple que puede ser entrenado de una sesión de 20 minutos. Hoy día, con el desarrollo de sensores de EEG cada vez menos aparatosos e invasivos, junto a técnicas de análisis casi instantáneas gracias al avance en potencia de computación, es posible construir sistemas portátiles para predecir el rendimiento basados en EEG. Por ello, creemos que nuestra investigación podría tener efectos prácticos superiores a los modelos complejos en la prevención de accidentes de tráfico.

7. Conclusiones

Los factores circadianos, como el cronotipo y la hora del día, juegan un papel importante en la ejecución durante la conducción, y es importante tenerlos en cuenta a la hora de desarrollar sistemas de prevención de accidentes.

Tanto el análisis de frecuencias del EEG como la temperatura corporal periférica son índices prometedores para predecir las fluctuaciones de la atención en tareas de vigilancia. Si bien el registro de la temperatura puede realizarse de forma más sencilla, barata y menos invasiva, su pobre resolución temporal en comparación al EEG, no la hacen idónea para un sistema de control de fatiga inmediato, aunque puede ser un buen indicador del nivel de atención global o incluso, un modificador del estado atencional.

La potencia en las bandas de frecuencia theta y alfa del EEG pueden predecir con hasta 2 segundos de antelación los tiempos de reacción en tareas que miden vigilancia, como la PVT o tareas de conducción simulada. El análisis de fuentes por el que se obtienen las áreas donde se originan los ritmos estudiados, confirma que estas fluctuaciones de potencia se corresponden con zonas de la red fronto-parietal atencional y la red por defecto, lo que sugiere su relación con los lapsos de atención y el decremento de vigilancia que se producen durante la realización de esta tarea. Esta dinámica de potencias y la localización de las fuentes que la produce es similar en la PVT y en la tarea de conducción, lo que sugiere que los

procesos subyacentes son similares y, por lo tanto, un modelo predictivo de la ejecución obtenido en una tarea es potencialmente extrapolable a la otra tarea.

Nuestro modelo predictivo basado en una regresión lineal funcionó para, aproximadamente, un tercio de los sujetos. Este resultado podría implicar que, si bien hay procesos similares entre ambas tareas y pueden ser usados para extrapolar el modelo en algunos sujetos, para poder obtener una generalización mayor del modelo habría que considerar las interacciones entre los distintos procesos atencionales (i.e., los relacionados con la tarea y los relacionados con la red por defecto) en lugar de verlos por separado.

Por tanto, en esta tesis, realizamos una serie de aportaciones con el fin de aumentar la seguridad en tareas que requieran vigilancia, en general, y en la conducción, en particular. Para ello, explicamos el efecto de los factores circadianos en la conducción, analizamos las dinámicas del EEG y de la temperatura como índices de ejecución en una tarea de vigilancia y proponemos un modelo de predicción de fatiga basado en estos índices y transferible entre distintas tareas atencionales.

Referencias

- Adan, A., & Almirall, H. (1991). Horne & Östberg morningness-eveningness questionnaire: A reduced scale. *Personality and Individual Differences, 12*(3), 241–253. [https://doi.org/10.1016/0191-8869\(91\)90110-W](https://doi.org/10.1016/0191-8869(91)90110-W)
- Adan, A., Archer, S. N., Hidalgo, M. P., Di Milia, L., Natale, V., & Randler, C. (2012). Circadian typology: a comprehensive review. *Chronobiology International, 29*(9), 1153–1175. <https://doi.org/10.3109/07420528.2012.719971>
- Akerstedt, T., Ingre, M., Kecklund, G., Anund, A., Sandberg, D., Wahde, M., ... Kronberg, P. (2010). Reaction of sleepiness indicators to partial sleep deprivation, time of day and time on task in a driving simulator--the DROWSI project. *Journal of Sleep Research, 19*(2), 298–309. <https://doi.org/10.1111/j.1365-2869.2009.00796.x>
- Arjunan, S. P., Kumar, D. K., & Tzyy-Ping Jung, T.-P. (2009). Changes in decibel scale wavelength properties of EEG with alertness levels while performing sustained attention tasks. In *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society* (Vol. 2009, pp. 6288–6291). IEEE. <https://doi.org/10.1109/IEMBS.2009.5332801>
- Aston-Jones, G. (2005). Brain structures and receptors involved in alertness. *Sleep Medicine, 6 Suppl 1*, S3-7. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16140243>
- Aston-Jones, G., Chen, S., Zhu, Y., & Oshinsky, M. L. (2001). A neural circuit for circadian regulation of arousal. *Nature Neuroscience, 4*(7), 732–738. <https://doi.org/10.1038/89522>
- Aue, W. R., Arruda, J. E., Kass, S. J., & Stanny, C. J. (2009). Cyclic variations in sustained human performance. *Brain and Cognition, 71*(3), 336–344. <https://doi.org/10.1016/j.bandc.2009.07.002>
- Babkoff, H., Zukerman, G., Fostick, L., & Ben-Artzi, E. (2005). Effect of the diurnal rhythm and 24 h of sleep deprivation on dichotic temporal order judgment. *Journal of Sleep Research, 14*(1), 7–15. <https://doi.org/10.1111/j.1365-2869.2004.00423.x>
- Baker, F. C., Driver, H. S., Paiker, J., Rogers, G. G., & Mitchell, D. (2002).

Acetaminophen does not affect 24-h body temperature or sleep in the luteal phase of the menstrual cycle. *Journal of Applied Physiology (Bethesda, Md. : 1985)*, 92(4), 1684–1691. <https://doi.org/10.1152/jappphysiol.00919.2001>

Baker, F., & Colrain, I. (2010). Daytime sleepiness, psychomotor performance, waking EEG spectra and evoked potentials in women with severe premenstrual syndrome. *Journal of Sleep Research*, 19(650), 214–227. <https://doi.org/10.1111/j.1365-2869.2009.00782.x>. Daytime

Balkin, T. J., & Wesensten, N. J. (2011). Differentiation of sleepiness and mental fatigue effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 47–66). Washington: American Psychological Association. <https://doi.org/10.1037/12343-002>

Basner, M., & Dinges, D. F. (2011). Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. *Sleep*, 34(5), 581–591. Retrieved from <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3079937&tool=pmcentrez&rendertype=abstract>

Basner, M., Hermosillo, E., Nasrini, J., McGuire, S., Saxena, S., Moore, T. M., ... Dinges, D. F. (2018). Repeated Administration Effects on Psychomotor Vigilance Test Performance. *Sleep*, 41(1). <https://doi.org/10.1093/sleep/zsx187>

Basner, M., Mollicone, D., & Dinges, D. F. (2011). Validity and Sensitivity of a Brief Psychomotor Vigilance Test (PVT-B) to Total and Partial Sleep Deprivation. *Acta Astronautica*, 69(11–12), 949–959. <https://doi.org/10.1016/j.actaastro.2011.07.015>

Bastiaansen, M. C. M., Posthuma, D., Groot, P. F. C., & de Geus, E. J. C. (2002). Event-related alpha and theta responses in a visuo-spatial working memory task. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 113(12), 1882–1893. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12464325>

Baulk, S. D., Biggs, S. N., Reid, K. J., van den Heuvel, C. J., & Dawson, D. (2008). Chasing the silver bullet: measuring driver fatigue using simple and complex

- tasks. *Accident; Analysis and Prevention*, 40(1), 396–402.
<https://doi.org/10.1016/j.aap.2007.07.008>
- Bekhtereva, V., Sander, C., Forschack, N., Olbrich, S., Hegerl, U., & Müller, M. M. (2014). Effects of EEG-vigilance regulation patterns on early perceptual processes in human visual cortex. *Clinical Neurophysiology*, 125(1), 98–107.
<https://doi.org/10.1016/j.clinph.2013.06.019>
- Bell, A. J., & Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation*, 7(6), 1129–1159.
Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7584893>
- Berendes, H., Marte, E., Ertel, R., McCarthy, J., Anderson, J., & Halberg, F. (1960). Circadian physiologic rhythms and lowered blood 5- hydroxytryptamine in human subjects with defective mentality. *Physiologist*, (3), 20.
- Blatter, K., & Cajochen, C. (2007). Circadian rhythms in cognitive performance: methodological constraints, protocols, theoretical underpinnings. *Physiology & Behavior*, 90(2–3), 196–208. <https://doi.org/10.1016/j.physbeh.2006.09.009>
- Blatter, K., Graw, P., Münch, M., Knoblauch, V., Wirz-Justice, A., & Cajochen, C. (2006). Gender and age differences in psychomotor vigilance performance under differential sleep pressure conditions. *Behavioural Brain Research*, 168(2), 312–317. <https://doi.org/10.1016/j.bbr.2005.11.018>
- Borbély, A. A. (1982). A two process model of sleep regulation. *Human Neurobiology*, 1(3), 195–204. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7185792>
- Brookhuis, K. A., & de Waard, D. (1993). The use of psychophysiology to assess driver status. *Ergonomics*, 36(9), 1099–1110.
<https://doi.org/10.1080/00140139308967981>
- Caldwell, J. A., Prazinko, B., & Caldwell, J. L. (2003). Body posture affects electroencephalographic activity and psychomotor vigilance task performance in sleep-deprived subjects. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 114(1), 23–31. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12495760>

- Chin-Teng Lin, C.-T., Shu-Fang Tsai, S.-F., & Li-Wei Ko, L.-W. (2013). EEG-Based Learning System for Online Motion Sickness Level Estimation in a Dynamic Vehicle Environment. *IEEE Transactions on Neural Networks and Learning Systems*, 24(10), 1689–1700. <https://doi.org/10.1109/TNNLS.2013.2275003>
- Chin-Teng Lin, Ruei-Cheng Wu, Sheng-Fu Liang, Wen-Hung Chao, Yu-Jie Chen, & Tzyy-Ping Jung. (2005). EEG-based drowsiness estimation for safety driving using independent component analysis. *IEEE Transactions on Circuits and Systems I: Regular Papers*, 52(12), 2726–2738. <https://doi.org/10.1109/TCSI.2005.857555>
- Chua, E. C.-P., Tan, W.-Q., Yeo, S.-C., Lau, P., Lee, I., Mien, I. H., ... Gooley, J. J. (2012a). Heart rate variability can be used to estimate sleepiness-related decrements in psychomotor vigilance during total sleep deprivation. *Sleep*, 35(3), 325–334. <https://doi.org/10.5665/sleep.1688>
- Chua, E. C.-P., Tan, W.-Q., Yeo, S.-C., Lau, P., Lee, I., Mien, I. H., ... Gooley, J. J. (2012b). Heart Rate Variability Can Be Used to Estimate Sleepiness-related Decrements in Psychomotor Vigilance during Total Sleep Deprivation. *SLEEP*, 35(3), 325–334. <https://doi.org/10.5665/sleep.1688>
- Chuang, C.-H., Ko, L.-W., Jung, T.-P., & Lin, C.-T. (2014). Kinesthesia in a sustained-attention driving task. *NeuroImage*, 91, 187–202. <https://doi.org/10.1016/j.neuroimage.2014.01.015>
- Chuang, S.-W., Ko, L.-W., Lin, Y.-P., Huang, R.-S., Jung, T.-P., & Lin, C.-T. (2012). Co-modulatory spectral changes in independent brain processes are correlated with task performance. *NeuroImage*, 62(3), 1469–1477. <https://doi.org/10.1016/j.neuroimage.2012.05.035>
- Clayton, M. S., Yeung, N., & Cohen Kadosh, R. (2015). The roles of cortical oscillations in sustained attention. *Trends in Cognitive Sciences*, 19(4), 188–195. <https://doi.org/10.1016/j.tics.2015.02.004>
- Comon, P. (1994). Independent component analysis, A new concept? *Signal Processing*, 36(3), 287–314. [https://doi.org/10.1016/0165-1684\(94\)90029-9](https://doi.org/10.1016/0165-1684(94)90029-9)
- Correa, A., Molina, E., & Sanabria, D. (2014). Effects of chronotype and time of day

- on the vigilance decrement during simulated driving. *Accident; Analysis and Prevention*, 67C, 113–118. <https://doi.org/10.1016/j.aap.2014.02.020>
- Correa, A., Triviño, M., Pérez-Dueñas, C., Acosta, A., & Lupiáñez, J. (2010). Temporal preparation, response inhibition and impulsivity. *Brain and Cognition*, 73(3), 222–228.
- Craig, A., Tran, Y., Wijesuriya, N., & Nguyen, H. (2012). Regional brain wave activity changes associated with fatigue. *Psychophysiology*, 49(4), 574–582. <https://doi.org/10.1111/j.1469-8986.2011.01329.x>
- Datta, S., & MacLean, R. R. (2007). Neurobiological mechanisms for the regulation of mammalian sleep–wake behavior: Reinterpretation of historical evidence and inclusion of contemporary cellular and molecular evidence. *Neuroscience & Biobehavioral Reviews*, 31(5), 775–824. <https://doi.org/10.1016/j.NEUBIOREV.2007.02.004>
- Davidson, P. R., Jones, R. D., & Peiris, M. T. R. (2007). EEG-Based Lapse Detection With High Temporal Resolution. *IEEE Transactions on Biomedical Engineering*, 54(5), 832–839. <https://doi.org/10.1109/TBME.2007.893452>
- Davies, D. R., & Parasuraman, R. (1982). *The psychology of vigilance*. London: Academic Press.
- Dawson, D., & Reid, K. (1997). Fatigue, alcohol and performance impairment. *Nature*, 388(6639), 235. <https://doi.org/10.1038/40775>
- Debener, S., Ullsperger, M., Siegel, M., Fiehler, K., von Cramon, D. Y., & Engel, A. K. (2005). Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 25(50), 11730–11737. <https://doi.org/10.1523/JNEUROSCI.3286-05.2005>
- Deiber, M.-P., Missonnier, P., Bertrand, O., Gold, G., Fazio-Costa, L., Ibañez, V., & Giannakopoulos, P. (2007). Distinction between perceptual and attentional processing in working memory tasks: a study of phase-locked and induced oscillatory brain dynamics. *Journal of Cognitive Neuroscience*, 19(1), 158–172.

<https://doi.org/10.1162/jocn.2007.19.1.158>

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21.

<https://doi.org/10.1016/j.jneumeth.2003.10.009>

Delorme, A., Westerfield, M., & Makeig, S. (2007). Medial prefrontal theta bursts precede rapid motor responses during visual selective attention. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *27*(44), 11949–11959. <https://doi.org/10.1523/JNEUROSCI.3477-07.2007>

Di Milia, L., Smolensky, M. H., Costa, G., Howarth, H. D., Ohayon, M. M., & Philip, P. (2011). Demographic factors, fatigue, and driving accidents: An examination of the published literature. *Accident; Analysis and Prevention*, *43*(2), 516–532.

<https://doi.org/10.1016/j.aap.2009.12.018>

Dinges, D. F., Pack, F., Williams, K., Gillen, K. A., Powell, J. W., Ott, G. E., ... Pack, A. I. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep*, *20*(4), 267–277. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/9231952>

Dinges, D. F., & Powell, J. W. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments, & Computers*, *17*(6), 652–655.

<https://doi.org/10.3758/BF03200977>

Dobbie, K., & Australian Transport Safety Bureau. (2002). *Fatigue-related crashes : an analysis of fatigue-related crashes on Australian roads using an operational definition of fatigue*. Australian Transport Safety Bureau. Retrieved from

<https://trid.trb.org/view.aspx?id=682899>

Dorrian, J., Rogers, N., & Dinges, D. F. (2005). Psychomotor vigilance performance: A neurocognitive assay sensitive to sleep loss. In K. C (Ed.), *Sleep Deprivation: Clinical Issues, Pharmacology and Sleep Loss Effects*. (pp. 39–70). NY: Marcel Dekker, Inc.

- Drummond, S. P. a, Bischoff-Grethe, A., Dinges, D. F., Ayalon, L., Mednick, S. C., & Meloy, M. J. (2005). The neural basis of the psychomotor vigilance task. *Sleep*, 28(9), 1059–1068. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16268374>
- Ebrahimi, F., Mikaeili, M., Estrada, E., & Nazeran, H. (2008). Automatic sleep stage classification based on EEG signals by using neural networks and wavelet packet coefficients. In *2008 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society* (Vol. 2008, pp. 1151–1154). IEEE. <https://doi.org/10.1109/IEMBS.2008.4649365>
- Eichele, T., Debener, S., Calhoun, V. D., Specht, K., Engel, A. K., Hugdahl, K., ... Ullsperger, M. (2008). Prediction of human errors by maladaptive changes in event-related brain networks. *Proceedings of the National Academy of Sciences of the United States of America*, 105(16), 6173–6178. <https://doi.org/10.1073/pnas.0708965105>
- Eoh, H. J., Chung, M. K., & Kim, S.-H. (2005). Electroencephalographic study of drowsiness in simulated driving with sleep deprivation. *International Journal of Industrial Ergonomics*, 35(4), 307–320. <https://doi.org/10.1016/j.ergon.2004.09.006>
- Fernandes, R., Hatfield, J., & Soames Job, R. F. (2010). A systematic investigation of the differential predictors for speeding, drink-driving, driving while fatigued, and not wearing a seat belt, among young drivers. *Transportation Research Part F: Traffic Psychology and Behaviour*, 13(3), 179–196. <https://doi.org/10.1016/J.TRF.2010.04.007>
- Figueiro, M. G., Bierman, A., Plitnick, B., & Rea, M. S. (2009). Preliminary evidence that both blue and red light can induce alertness at night. *BMC Neuroscience*, 10(1), 105. <https://doi.org/10.1186/1471-2202-10-105>
- Finomore, V., Matthews, G., Shaw, T., & Warm, J. (2009). Predicting vigilance: a fresh look at an old problem. *Ergonomics*, 52(7), 791–808. <https://doi.org/10.1080/00140130802641627>
- Folkard, S. (1997). Black times: temporal determinants of transport safety.

Accident; Analysis and Prevention, 29(4), 417–430. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9248500>

Folkard, S., & Akerstedt, T. (1987). Towards a model for the prediction of alertness and/or fatigue on different sleep/wake schedules. In J. Oginski, A., Pokorski, J., & Rutenfranz (Ed.), *Contemporary advances in shiftwork research*. Krakow: Medical Academy.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences*, 102(27), 9673–9678. <https://doi.org/10.1073/pnas.0504136102>

González, N., Kalyakin, I., & Lyytinen, H. (2009). RACER: A Non-Commercial Driving Game which Became a Serious Tool in the Research of Driver Fatigue. In M. Kankaanranta & P. Neittaanmäki (Eds.), *Design and Use of Serious Games* (pp. 171–184).

Grandchamp, R., & Delorme, A. (2011). Single-trial normalization for event-related spectral decomposition reduces sensitivity to noisy trials. *Frontiers in Psychology*, 2, 236. <https://doi.org/10.3389/fpsyg.2011.00236>

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003a). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences*, 100(1), 253–258. <https://doi.org/10.1073/pnas.0135058100>

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003b). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences*, 100(1), 253–258. <https://doi.org/10.1073/pnas.0135058100>

Grier, R. A., Warm, J. S., Dember, W. N., Matthews, G., Galinsky, T. L., Szalma, J. L., & Parasuraman, R. (2003). The Vigilance Decrement Reflects Limitations in Effortful Attention, Not Mindlessness. *Human Factors: The Journal of the Human Factors and Ergonomics Society*, 45(3), 349–359. <https://doi.org/10.1518/hfes.45.3.349.27253>

- Gruber, W. R., Klimesch, W., Sauseng, P., & Doppelmayr, M. (2005). Alpha phase synchronization predicts P1 and N1 latency and amplitude size. *Cerebral Cortex (New York, N.Y. : 1991)*, *15*(4), 371–377.
<https://doi.org/10.1093/cercor/bhh139>
- Hallvig, D., Anund, A., Fors, C., Kecklund, G., Karlsson, J. G., Wahde, M., & Åkerstedt, T. (2013). Sleepy driving on the real road and in the simulator - A comparison. *Accident Analysis and Prevention*, *50*.
<https://doi.org/10.1016/j.aap.2012.09.033>
- Hasher, L., Chung, C., May, C. P., & Foong, N. (2002). Age, time of testing, and proactive interference. *Canadian Journal of Experimental Psychology = Revue Canadienne de Psychologie Experimentale*, *56*(3), 200–207. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12271750>
- Hastings, M. H., Reddy, A. B., & Maywood, E. S. (2003). A clockwork web: circadian timing in brain and periphery, in health and disease. *Nature Reviews Neuroscience*, *4*(8), 649–661. <https://doi.org/10.1038/nrn1177>
- Helton, W. S., & Warm, J. S. (2008). Signal salience and the mindlessness theory of vigilance. *Acta Psychologica*, *129*(1), 18–25.
<https://doi.org/10.1016/j.ACTPSY.2008.04.002>
- Hinds, O., Thompson, T. W., Ghosh, S., Yoo, J. J., Whitfield-Gabrieli, S., Triantafyllou, C., & Gabrieli, J. D. E. (2013). Roles of default-mode network and supplementary motor area in human vigilance performance: evidence from real-time fMRI. *Journal of Neurophysiology*, *109*(5), 1250–1258.
<https://doi.org/10.1152/jn.00533.2011>
- Hoedlmoser, K., Griessenberger, H., Fellingner, R., Freunberger, R., Klimesch, W., Gruber, W., & Schabus, M. (2011). Event-related activity and phase locking during a psychomotor vigilance task over the course of sleep deprivation. *Journal of Sleep Research*, *20*(3), 377–385. <https://doi.org/10.1111/j.1365-2869.2010.00892.x>
- Horne, J. A. (1993). Human sleep, sleep loss and behaviour. Implications for the prefrontal cortex and psychiatric disorder. *The British Journal of Psychiatry* :

- The Journal of Mental Science*, 162, 413–419. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8453439>
- Horne, J. A., & Reyner, L. A. (1995). Sleep related vehicle accidents. *BMJ (Clinical Research Ed.)*, 310(6979), 565–567. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7888930>
- Horne, J., & Östberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology*, 4(2), 97–110.
- Hornik, J., & Miniero, G. (2009). Synchrony effects on customers' responses and behaviors. *International Journal of Research in Marketing*, 26(1), 34–40. <https://doi.org/10.1016/J.IJRESMAR.2008.04.002>
- Huang, R.-S., Jung, T.-P., & Makeig, S. (2007). Event-related brain dynamics in continuous sustained-attention tasks, 65–74. Retrieved from <http://dl.acm.org/citation.cfm?id=1763088.1763097>
- Huang, R.-S., Jung, T.-P., & Makeig, S. (2009). Tonic changes in EEG power spectra during simulated driving. In D. D. Schmorow, I. V. Estabrooke, & M. Grootjen (Eds.), *Foundations of Augmented Cognition. Neuroergonomics and Operational Neuroscience* (pp. 394–403). Berlin, Heidelberg: Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-642-02812-0_47
- Huang, R., Jung, T., Delorme, A., & Makeig, S. (2008). Tonic and phasic electroencephalographic dynamics during continuous compensatory tracking. *NeuroImage*, 39(4), 1896–1909. <https://doi.org/10.1016/j.neuroimage.2007.10.036>
- Ingre, M., Akerstedt, T., Peters, B., Anund, A., & Kecklund, G. (2006). Subjective sleepiness, simulated driving performance and blink duration: examining individual differences. *Journal of Sleep Research*, 15(1), 47–53. <https://doi.org/10.1111/j.1365-2869.2006.00504.x>
- Jackson, M. L., Croft, R. J., Kennedy, G. A., Owens, K., & Howard, M. E. (2012). Cognitive components of simulated driving performance: Sleep loss effects and predictors. *Accident; Analysis and Prevention*.

<https://doi.org/10.1016/j.aap.2012.05.020>

- Jennings, J. R., & Wood, C. C. (1976). The e-adjustment procedure for repeated-measures analyses of variance. *Psychophysiology*, *13*, 277–278.
- Jensen, B. K. (1982). Menstrual cycle effects on task performance examined in the context of stress research. *Acta Psychologica*, *50*(2), 159–178. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7201734>
- Jiang, J. (2007). *Linear and Generalized Linear Mixed Models and Their Applications*. New York, NY: Springer New York. <https://doi.org/10.1007/978-0-387-47946-0>
- Jung, T. P., Makeig, S., Stensmo, M., & Sejnowski, T. J. (1997). Estimating alertness from the EEG power spectrum. *IEEE Transactions on Bio-Medical Engineering*, *44*(1), 60–69. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9214784>
- Kang, H.-B. (2013). Various Approaches for Driver and Driving Behavior Monitoring: A Review. In *2013 IEEE International Conference on Computer Vision Workshops* (pp. 616–623). IEEE. <https://doi.org/10.1109/ICCVW.2013.85>
- Käthner, I., Wriessnegger, S. C., Müller-Putz, G. R., Kübler, A., & Halder, S. (2014). Effects of mental workload and fatigue on the P300, alpha and theta band power during operation of an ERP (P300) brain-computer interface. *Biological Psychology*. <https://doi.org/10.1016/j.biopsycho.2014.07.014>
- Katzenberg, D., Young, T., Finn, L., Lin, L., King, D. P., Takahashi, J. S., & Mignot, E. (1998). A CLOCK polymorphism associated with human diurnal preference. *Sleep*, *21*(6), 569–576.
- Kecklund, G., & Akerstedt, T. (1993). Sleepiness in long distance truck driving: an ambulatory EEG study of night driving. *Ergonomics*, *36*(9), 1007–1017. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8404830>
- Keenan, P. A., Lindamer, L. A., & Jong, S. K. (1995). Menstrual phase-independent retrieval deficit in women with PMS. *Biological Psychiatry*, *38*(6), 369–377. [https://doi.org/10.1016/0006-3223\(94\)00303-K](https://doi.org/10.1016/0006-3223(94)00303-K)

- Kerkhof, G. A., & Van Dongen, H. P. (1996). Morning-type and evening-type individuals differ in the phase position of their endogenous circadian oscillator. *Neuroscience Letters*, *218*(3), 153–156.
- Kleitman, N. (1933). Studies on the physiology of sleep: VIII. Diurnal Variation in Performance. *American Journal of Physiology -- Legacy Content*, *104*(2), 449–456.
- Kleitman, N., Titelbaum, S., & Feiveson, P. (1938). The effect of body temperature on reaction time. *American Journal of Physiology*, *121*(2), 495–501. Retrieved from <http://ajplegacy.physiology.org/content/121/2/495>
- Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research. Brain Research Reviews*, *29*(2–3), 169–195. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10209231>
- Klimesch, W., Doppelmayr, M., Russegger, H., Pachinger, T., & Schwaiger, J. (1998). Induced alpha band power changes in the human EEG and attention. *Neuroscience Letters*, *244*(2), 73–76. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9572588>
- Kräuchi, K. (2007). The human sleep-wake cycle reconsidered from a thermoregulatory point of view. *Physiology & Behavior*, *90*(2–3), 236–245. <https://doi.org/10.1016/j.physbeh.2006.09.005>
- Lal, S. K. L., & Craig, A. (2001). A critical review of the psychophysiology of driver fatigue. *Biological Psychology*, *55*(3), 173–194. [https://doi.org/10.1016/S0301-0511\(00\)00085-5](https://doi.org/10.1016/S0301-0511(00)00085-5)
- Lal, S. K. L., & Craig, A. (2002). Driver fatigue: electroencephalography and psychological assessment. *Psychophysiology*, *39*(3), 313–321. <https://doi.org/10.1017.S0048577201393095>
- Lara, T., Madrid, J., & Correa, A. (n.d.). Effects of time of day and chronotype on vigilance and executive control. *PLoS ONE*.
- Lara, T., Molina, E., Madrid, J. A., & Correa, Á. (2018). Electroencephalographic and skin temperature indices of vigilance and inhibitory control. *Psicológica*

Journal. <https://doi.org/10.2478/psicolj-2018-0010>

Laukka, S. J., Järvillehto, T., Alexandrov, Y. I., & Lindqvist, J. (1995). Frontal midline theta related to learning in a simulated driving task. *Biological Psychology*, *40*(3), 313–320. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/7669839>

Lavie, P. (1986). Ultrashort sleep-waking schedule. III. “Gates” and “forbidden zones” for sleep. *Electroencephalography and Clinical Neurophysiology*, *63*(5), 414–425.

Lenné, M. G., Triggs, T. J., & Redman, J. R. (1997). Time of day variations in driving performance. *Accid Anal Prev*, *29*(4), 431–437.

[https://doi.org/10.1016/S0001-4575\(97\)00022-5](https://doi.org/10.1016/S0001-4575(97)00022-5)

Lenné, M. G., Triggs, T. J., & Redman, J. R. (1997). Time of day variations in driving performance. *Accident; Analysis and Prevention*, *29*(4), 431–437. Retrieved

from <http://www.ncbi.nlm.nih.gov/pubmed/9248501>

Lim, J., & Dinges, D. F. (2008). Sleep deprivation and vigilant attention. *Annals of the New York Academy of Sciences*, *1129*, 305–322.

<https://doi.org/10.1196/annals.1417.002>

Lin, C.-T., Chuang, C.-H., Wang, Y.-K., Tsai, S.-F., Chiu, T.-C., & Ko, L.-W. (2012).

Neurocognitive Characteristics of the Driver: A Review on Drowsiness, Distraction, Navigation, and Motion Sickness. *Journal of Neuroscience and Neuroengineering*, *1*(1), 61–81. <https://doi.org/10.1166/jnsne.2012.1010>

Lin, C.-T., Huang, K.-C., Chao, C.-F., Chen, J.-A., Chiu, T.-W., Ko, L.-W., & Jung, T.-P. (2010). Tonic and phasic EEG and behavioral changes induced by arousing

feedback. *NeuroImage*, *52*(2), 633–642.

<https://doi.org/10.1016/j.neuroimage.2010.04.250>

Lin, C.-T., Ko, L.-W., Chung, I.-F., Huang, T.-Y., Chen, Y.-C., Jung, T.-P., & Liang, S.-F. (2006). Adaptive EEG-Based Alertness Estimation System by Using ICA-Based

Fuzzy Neural Networks. *IEEE Transactions on Circuits and Systems I: Regular Papers*, *53*(11), 2469–2476. <https://doi.org/10.1109/TCSI.2006.884408>

Lin, F.-C., Ko, L.-W., Chuang, C.-H., Su, T.-P., & Lin, C.-T. (2012). Generalized EEG-

Based Drowsiness Prediction System by Using a Self-Organizing Neural Fuzzy System. *IEEE Transactions on Circuits and Systems I: Regular Papers*, 59(9), 2044–2055. <https://doi.org/10.1109/TCSI.2012.2185290>

Liu, Y. T., Lin, Y. Y., Wu, S. L., Chuang, C. H., & Lin, C. T. (2016). Brain Dynamics in Predicting Driving Fatigue Using a Recurrent Self-Evolving Fuzzy Neural Network. *IEEE Transactions on Neural Networks and Learning Systems*, 27(2). <https://doi.org/10.1109/TNNLS.2015.2496330>

Lo, S., & Andrews, S. (2015). To transform or not to transform: using generalized linear mixed models to analyse reaction time data. *Frontiers in Psychology*, 6, 1171. <https://doi.org/10.3389/fpsyg.2015.01171>

Loftus, G. R. (1978). On interpretation of interactions. *Memory & Cognition*, 6(3), 312–319. <https://doi.org/10.3758/BF03197461>

Mackworth, N. H. (1948). The breakdown of vigilance during prolonged visual search. *Quarterly Journal of Experimental Psychology*, 1, 6–21.

MacLean, A. W., Davies, D. R. ., & Thiele, K. (2003). The hazards and prevention of driving while sleepy. *Sleep Medicine Reviews*, 7(6), 507–521. [https://doi.org/10.1016/S1087-0792\(03\)90004-9](https://doi.org/10.1016/S1087-0792(03)90004-9)

Makeig, S. (1993). Auditory event-related dynamics of the EEG spectrum and effects of exposure to tones. *Electroencephalography and Clinical Neurophysiology*, 86(4), 283–293. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7682932>

Makeig, S., Bell, A. J., Jung, T.-P., & Sejnowski, T. J. (1996). Independent Component Analysis of Electroencephalographic Data, (3), 145–151.

Makeig, S., Delorme, A., Westerfield, M., Jung, T.-P., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2004). Electroencephalographic brain dynamics following manually responded visual targets. *PLoS Biology*, 2(6), e176. <https://doi.org/10.1371/journal.pbio.0020176>

Makeig, S., Jung, T. P., Bell, A. J., Ghahremani, D., & Sejnowski, T. J. (1997). Blind separation of auditory event-related brain responses into independent components. *Proceedings of the National Academy of Sciences of the United*

States of America, 94(20), 10979–10984. Retrieved from <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=23551&tool=pmcentrez&rendertype=abstract>

Makeig, S., Westerfield, M., Jung, T. P., Enghoff, S., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2002). Dynamic brain sources of visual evoked responses. *Science (New York, N.Y.)*, 295(5555), 690–694. <https://doi.org/10.1126/science.1066168>

Mardi, Z., Ashtiani, S. N. M., & Mikaili, M. (2011). EEG-based Drowsiness Detection for Safe Driving Using Chaotic Features and Statistical Tests. *Journal of Medical Signals and Sensors*, 1(2), 130–137. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22606668>

Martel, A., Dähne, S., & Blankertz, B. (2014). EEG predictors of covert vigilant attention. *Journal of Neural Engineering*, 11(3), 035009. <https://doi.org/10.1088/1741-2560/11/3/035009>

Martin, J. S., Hébert, M., Ledoux, É., Gaudreault, M., & Laberge, L. (2012). Relationship of Chronotype to Sleep, Light Exposure, and Work-Related Fatigue in Student Workers. *Chronobiology International*, 29(3), 295–304. <https://doi.org/10.3109/07420528.2011.653656>

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: the default network and stimulus-independent thought. *Science (New York, N.Y.)*, 315(5810), 393–395. <https://doi.org/10.1126/science.1131295>

Matthews, R. W., Ferguson, S. A., Zhou, X., Sargent, C., Darwent, D., Kennaway, D. J., & Roach, G. D. (2012). Time-of-day mediates the influences of extended wake and sleep restriction on simulated driving. *Chronobiology International*, 29(5), 572–579. <https://doi.org/10.3109/07420528.2012.675845>

May, C. P., & Hasher, L. (1998). Synchrony effects in inhibitory control over thought and action. *Journal of Experimental Psychology. Human Perception and Performance*, 24(2), 363–379. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9554091>

- May, J. F., & Baldwin, C. L. (2009). Driver fatigue: The importance of identifying causal factors of fatigue when considering detection and countermeasure technologies. *Transportation Research Part F: Traffic Psychology and Behaviour*, *12*(3), 218–224. <https://doi.org/10.1016/J.TRF.2008.11.005>
- Mesulam, M.-M. (1990). Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Annals of Neurology*, *28*(5), 597–613. <https://doi.org/10.1002/ana.410280502>
- Monk, T. H. (1989). A visual analogue scale technique to measure global vigor and affect. *Psychiatry Research*, *27*(1), 89–99. [https://doi.org/10.1016/0165-1781\(89\)90013-9](https://doi.org/10.1016/0165-1781(89)90013-9)
- Monk, T. H., & Leng, V. C. (1986). Interactions between inter-individual and inter-task differences in the diurnal variation of human performance. *Chronobiology International*, *3*(3), 171–177. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3677200>
- Morgan, M., & Rapkin, A. (2012). Cognitive flexibility, reaction time, and attention in women with premenstrual dysphoric disorder. *The Journal of Gender-Specific Medicine : JGSM : The Official Journal of the Partnership for Women's Health at Columbia*, *5*(3), 28–36. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12078060>
- Mountcastle, V. B. (1978). Brain mechanisms for directed attention. *Journal of the Royal Society of Medicine*, *71*(1), 14–28. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/416210>
- Mullaney, D. J., Kripke, D. F., Fleck, P. A., & Johnson, L. C. (1983). Sleep loss and nap effects on sustained continuous performance. *Psychophysiology*, *20*(6), 643–651. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6657852>
- Nolan, H., Whelan, R., & Reilly, R. B. (2010). FASTER: Fully Automated Statistical Thresholding for EEG artifact Rejection. *Journal of Neuroscience Methods*, *192*(1), 152–162. <https://doi.org/10.1016/j.jneumeth.2010.07.015>
- Oginska, H., Fafrowicz, M., Golonka, K., Marek, T., Mojsa-Kaja, J., & Tucholska, K. (2010). Chronotype, sleep loss, and diurnal pattern of salivary cortisol in a

- simulated daylong driving. *Chronobiology International*, 27(5), 959–974.
<https://doi.org/10.3109/07420528.2010.489412>
- Oken, B. S., Salinsky, M. C., & Elsas, S. M. (2006). Vigilance, alertness, or sustained attention: physiological basis and measurement. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 117(9), 1885–1901. <https://doi.org/10.1016/j.clinph.2006.01.017>
- Okogbaa, O. G., Shell, R. L., & Filipusic, D. (1994). On the investigation of the neurophysiological correlates of knowledge worker mental fatigue using the EEG signal. *Applied Ergonomics*, 25(6), 355–365. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15676987>
- Onton, J., Delorme, A., & Makeig, S. (2005). Frontal midline EEG dynamics during working memory. *NeuroImage*, 27(2), 341–356.
<https://doi.org/10.1016/j.neuroimage.2005.04.014>
- Onton, J., & Makeig, S. (2006). Information-based modeling of event-related brain dynamics. *Progress in Brain Research*, 159, 99–120.
[https://doi.org/10.1016/S0079-6123\(06\)59007-7](https://doi.org/10.1016/S0079-6123(06)59007-7)
- Onton, J., & Makeig, S. (2009). High-frequency Broadband Modulations of Electroencephalographic Spectra. *Frontiers in Human Neuroscience*, 3, 61.
<https://doi.org/10.3389/neuro.09.061.2009>
- Onton, J., Westerfield, M., Townsend, J., & Makeig, S. (2006). Imaging human EEG dynamics using independent component analysis. *Neuroscience and Biobehavioral Reviews*, 30(6), 808–822.
<https://doi.org/10.1016/j.neubiorev.2006.06.007>
- Oostenveld, R., & Oostendorp, T. F. (2002). Validating the boundary element method for forward and inverse EEG computations in the presence of a hole in the skull. *Human Brain Mapping*, 17(3), 179–192.
<https://doi.org/10.1002/hbm.10061>
- Otmani, S., Pebayle, T., Roge, J., & Muzet, A. (2005). Effect of driving duration and partial sleep deprivation on subsequent alertness and performance of car drivers. *Physiology & Behavior*, 84(5), 715–724.

<https://doi.org/10.1016/j.physbeh.2005.02.021>

Otmani, S., Rogé, J., & Muzet, A. (2005). Sleepiness in professional drivers: effect of age and time of day. *Accident; Analysis and Prevention*, *37*(5), 930–937.

<https://doi.org/10.1016/j.aap.2005.04.011>

Parasuraman, R. (1998). *The attentive brain*. Cambridge, MA: The MIT Press.

Perrier, J., Jongen, S., Vuurman, E., Bocca, M. L., Ramaekers, J. G., & Vermeeren, A. (2016). Driving performance and EEG fluctuations during on-the-road driving following sleep deprivation. *Biological Psychology*, *121*, 1–11.

<https://doi.org/10.1016/j.biopsycho.2016.09.010>

Pfurtscheller, G. (1992). Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. *Electroencephalography and Clinical Neurophysiology*, *83*(1), 62–69. [https://doi.org/10.1016/0013-4694\(92\)90133-3](https://doi.org/10.1016/0013-4694(92)90133-3)

Pfurtscheller, G., & Berghold, A. (1989). Patterns of cortical activation during planning of voluntary movement. *Electroencephalography and Clinical Neurophysiology*, *72*(3), 250–258. [https://doi.org/10.1016/0013-4694\(89\)90250-2](https://doi.org/10.1016/0013-4694(89)90250-2)

Pfurtscheller, G., Neuper, C., Andrew, C., & Edlinger, G. (1997). Foot and hand area mu rhythms. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology*, *26*(1–3), 121–135. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9202999>

Pfurtscheller, G., Neuper, C., & Krausz, G. (2000). Functional dissociation of lower and upper frequency mu rhythms in relation to voluntary limb movement. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *111*(10), 1873–1879. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11018505>

Phillips, R. O. (2015). A review of definitions of fatigue – And a step towards a whole definition. *Transportation Research Part F: Traffic Psychology and Behaviour*, *29*, 48–56. <https://doi.org/10.1016/J.TRF.2015.01.003>

Phipps-Nelson, J., Redman, J. R., Dijk, D.-J., & Rajaratnam, S. M. W. (2003). Daytime

exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep*, 26(6), 695–700.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14572122>

Phipps-Nelson, J., Redman, J. R., Schlangen, L. J. M., & Rajaratnam, S. M. W. (2009). Blue light exposure reduces objective measures of sleepiness during prolonged nighttime performance testing. *Chronobiology International*, 26(5), 891–912. <https://doi.org/10.1080/07420520903044364>

Pilcher, J. J., Band, D., Odle-Dusseau, H. N., & Muth, E. R. (2007). Human performance under sustained operations and acute sleep deprivation conditions: toward a model of controlled attention. *Aviation, Space, and Environmental Medicine*, 78(5 Suppl), B15-24. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17547301>

Posner, M. I., & Petersen, S. E. (1990). The Attention System of the Human Brain. *Annual Review of Neuroscience*, 13(1), 25–42.

<https://doi.org/10.1146/annurev.ne.13.030190.000325>

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences*, 98(2), 676–682.

<https://doi.org/10.1073/pnas.98.2.676>

Rajaratnam, S. M., & Arendt, J. (2001). Health in a 24-h society. *The Lancet*, 358(9286), 999–1005. [https://doi.org/10.1016/S0140-6736\(01\)06108-6](https://doi.org/10.1016/S0140-6736(01)06108-6)

Ralph, M. R., Foster, R. G., Davis, F. C., & Menaker, M. (1990). Transplanted suprachiasmatic nucleus determines circadian period. *Science (New York, N.Y.)*, 247(4945), 975–978. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/2305266>

Ramautar, J. R., Romeijn, N., Gómez-Herrero, G., Piantoni, G., & Van Someren, E. J. W. (2013). Coupling of infraslow fluctuations in autonomic and central vigilance markers: skin temperature, EEG beta power and ERP P300 latency. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, 89(2), 158–164.

<https://doi.org/10.1016/j.ijpsycho.2013.01.001>

- Ranney, T. A., Simmons, L. A., & Masalonis, A. J. (1999). Prolonged exposure to glare and driving time: effects on performance in a driving simulator. *Accident; Analysis and Prevention*, *31*(6), 601–610.
- Raymann, R. J. E. M., & Van Someren, E. J. W. (2007). Time-on-task impairment of psychomotor vigilance is affected by mild skin warming and changes with aging and insomnia. *Sleep*, *30*(1), 96–103. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17310870>
- Raz, A., & Buhle, J. (2006). Typologies of attentional networks. *Nature Reviews. Neuroscience*, *7*(5), 367–379. <https://doi.org/10.1038/nrn1903>
- Reinke, L., Özbay, Y., Dieperink, W., & Tulleken, J. E. (2015). The effect of chronotype on sleepiness, fatigue, and psychomotor vigilance of ICU nurses during the night shift. *Intensive Care Medicine*, *41*(4), 657–666. <https://doi.org/10.1007/s00134-015-3667-7>
- Retey, J. V., Adam, M., Gottselig, J. M., Khatami, R., Durr, R., Achermann, P., & Landolt, H.-P. (2006). Adenosinergic Mechanisms Contribute to Individual Differences in Sleep Deprivation-Induced Changes in Neurobehavioral Function and Brain Rhythmic Activity. *Journal of Neuroscience*, *26*(41), 10472–10479. <https://doi.org/10.1523/JNEUROSCI.1538-06.2006>
- Reyner, L. A., & Horne, J. A. (1998). Falling asleep whilst driving: are drivers aware of prior sleepiness? *International Journal of Legal Medicine*, *111*(3), 120–123.
- Robertson, I. H., Manly, T., Andrade, J., Baddeley, B. T., & Yiend, J. (1997). “Oops!”: performance correlates of everyday attentional failures in traumatic brain injured and normal subjects. *Neuropsychologia*, *35*(6), 747–758. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9204482>
- Romeijn, N., Raymann, R. J. E. M., Møst, E., Te Lindert, B., Van Der Meijden, W. P., Fronczek, R., ... Van Someren, E. J. W. (2012). Sleep, vigilance, and thermosensitivity. *Pflügers Archiv : European Journal of Physiology*, *463*(1), 169–176. <https://doi.org/10.1007/s00424-011-1042-2>
- Romeijn, N., & Van Someren, E. J. W. (2011). Correlated fluctuations of daytime skin

- temperature and vigilance. *Journal of Biological Rhythms*, 26(1), 68–77.
<https://doi.org/10.1177/0748730410391894>
- Romeijn, N., Verweij, I. M., Koeleman, A., Mooij, A., Steimke, R., Virkkala, J., ... Van Someren, E. J. W. (2012). Cold hands, warm feet: sleep deprivation disrupts thermoregulation and its association with vigilance. *Sleep*, 35(12), 1673–1683.
<https://doi.org/10.5665/sleep.2242>
- Rowe, G., Hasher, L., & Turcotte, J. (2009). Short article: Age and synchrony effects in visuospatial working memory. *Quarterly Journal of Experimental Psychology*, 62(10), 1873–1880.
<https://doi.org/10.1080/17470210902834852>
- Saper, C. B., Scammell, T. E., & Lu, J. (2005). Hypothalamic regulation of sleep and circadian rhythms. *Nature*, 437(7063), 1257–1263.
<https://doi.org/10.1038/nature04284>
- Schneider, W., Eschman, A., & Zuccolotto, A. (2001). *E-Prime User's Guide*. Pittsburgh: Psychology Software Tools, Inc.
- Sergeant, J., Geuze, R., & van Winsum, W. (1987). Event-related desynchronization and P300. *Psychophysiology*, 24(3), 272–277. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3602282>
- Shechter, A., Boudreau, P., Varin, F., & Boivin, D. B. (2011). Predominance of distal skin temperature changes at sleep onset across menstrual and circadian phases. *Journal of Biological Rhythms*, 26(3), 260–270.
<https://doi.org/10.1177/0748730411404677>
- Shekleton, J. A., Rajaratnam, S. M. W., Gooley, J. J., Van Reen, E., Czeisler, C. A., & Lockley, S. W. (2013). Improved neurobehavioral performance during the wake maintenance zone. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine*, 9(4), 353–362.
<https://doi.org/10.5664/jcsm.2588>
- Shibui, K., Uchiyama, M., Okawa, M., Kudo, Y., Kim, K., Liu, X., ... Ishibashi, K. (2000). Diurnal fluctuation of sleep propensity and hormonal secretion across the menstrual cycle. *Biological Psychiatry*, 48(11), 1062–1068. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/11094139>

Shou, G., & Ding, L. (2013). Frontal theta EEG dynamics in a real-world air traffic control task. *Conference Proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference, 2013*, 5594–5597.
<https://doi.org/10.1109/EMBC.2013.6610818>

Siegel, J. (2004). Brain mechanisms that control sleep and waking. *Naturwissenschaften*, 91(8), 355–365. <https://doi.org/10.1007/s00114-004-0541-9>

Smallwood, J., & Schooler, J. W. (2006). The restless mind. *Psychological Bulletin*, 132(6), 946–958. <https://doi.org/10.1037/0033-2909.132.6.946>

Smith, K. J., Valentino, D. A., & Arruda, J. E. (2003). Rhythmic Oscillations in the Performance of a Sustained Attention Task. *Journal of Clinical and Experimental Neuropsychology (Neuropsychology, Development and Cognition: Section A)*, 25(4), 561–570. <https://doi.org/10.1076/jcen.25.4.561.13869>

Stikic, M., Johnson, R. R., Levendowski, D. J., Popovic, D. P., Olmstead, R. E., & Berka, C. (2011). EEG-derived estimators of present and future cognitive performance. *Frontiers in Human Neuroscience*, 5, 70.
<https://doi.org/10.3389/fnhum.2011.00070>

Thomson, D. R., Besner, D., & Smilek, D. (2015). A resource-control account of sustained attention: evidence from mind-wandering and vigilance paradigms. *Perspectives on Psychological Science : A Journal of the Association for Psychological Science*, 10(1), 82–96.
<https://doi.org/10.1177/1745691614556681>

Ting, P.-H., Hwang, J.-R., Doong, J.-L., & Jeng, M.-C. (2008a). Driver fatigue and highway driving: a simulator study. *Physiology & Behavior*, 94(3), 448–453.
<https://doi.org/10.1016/j.physbeh.2008.02.015>

Ting, P.-H., Hwang, J.-R., Doong, J.-L., & Jeng, M.-C. (2008b). Driver fatigue and highway driving: A simulator study. *Physiology & Behavior*, 94(3), 448–453.
<https://doi.org/10.1016/j.physbeh.2008.02.015>

- Touryan, J., Apker, G., Lance, B. J., Kerick, S. E., Ries, A. J., & McDowell, K. (2014). Estimating endogenous changes in task performance from EEG. *Frontiers in Neuroscience*, *8*, 155. <https://doi.org/10.3389/fnins.2014.00155>
- Touryan, J., Lance, B. J., Kerick, S. E., Ries, A. J., & McDowell, K. (2016). Common EEG features for behavioral estimation in disparate, real-world tasks. *Biological Psychology*, *114*, 93–107. <https://doi.org/10.1016/j.biopsycho.2015.12.009>
- Tucker, D. M., Liotti, M., Potts, G. F., Russell, G. S., & Posner, M. I. (1994). Spatiotemporal analysis of brain electrical fields. *Human Brain Mapping*, *1*(2), 134–152. <https://doi.org/10.1002/hbm.460010206>
- Valdez, P., Ramírez, C., García, A., Talamantes, J., & Cortez, J. (2010). Circadian and homeostatic variation in sustained attention. *Chronobiology International*, *27*(2), 393–416. <https://doi.org/10.3109/07420521003765861>
- Valentino, D. A., Arruda, J. E., & Gold, S. M. (1993). Comparison of QEEG and response accuracy in good vs poorer performers during a vigilance task. *International Journal of Psychophysiology*, *15*(2), 123–133. [https://doi.org/10.1016/0167-8760\(93\)90070-6](https://doi.org/10.1016/0167-8760(93)90070-6)
- Van Dongen, H. P. A., Baynard, M. D., Maislin, G., & Dinges, D. F. (2004). Systematic interindividual differences in neurobehavioral impairment from sleep loss: evidence of trait-like differential vulnerability. *Sleep*, *27*(3), 423–433. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15164894>
- Van Someren, E. J. W. (2006). Mechanisms and functions of coupling between sleep and temperature rhythms. In *Progress in brain research* (Vol. 153, pp. 309–324). [https://doi.org/10.1016/S0079-6123\(06\)53018-3](https://doi.org/10.1016/S0079-6123(06)53018-3)
- Van Winsum, W., Sergeant, J., & Geuze, R. (1984). The functional significance of event-related desynchronization of alpha rhythm in attentional and activating tasks. *Electroencephalography and Clinical Neurophysiology*, *58*(6), 519–524. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6209102>
- von Stein, A., & Sarnthein, J. (2000). Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization. *International Journal of Psychophysiology : Official Journal of*

the International Organization of Psychophysiology, 38(3), 301–313. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11102669>

- Vuckovic, A., Radivojevic, V., Chen, A. C. N., & Popovic, D. (2002). Automatic recognition of alertness and drowsiness from EEG by an artificial neural network. *Medical Engineering & Physics*, 24(5), 349–360. [https://doi.org/10.1016/S1350-4533\(02\)00030-9](https://doi.org/10.1016/S1350-4533(02)00030-9)
- Waag, W. L., Halcomb, C. G., & Tyler, D. M. (1973). Sex differences in monitoring performance. *Journal of Applied Psychology*, 58(2), 272–274. <https://doi.org/10.1037/h0035516>
- Wang, J., Sun, S., Fang, S., Fu, T., & Stipanovic, J. (2017). Predicting drowsy driving in real-time situations: Using an advanced driving simulator, accelerated failure time model, and virtual location-based services. *Accident Analysis and Prevention*, 99. <https://doi.org/10.1016/j.aap.2016.12.014>
- Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. *Nature Neuroscience*, 9(7), 971–978. <https://doi.org/10.1038/nn1727>
- Williamson, A., Lombardi, D. a, Folkard, S., Stutts, J., Courtney, T. K., & Connor, J. L. (2011). The link between fatigue and safety. *Accident; Analysis and Prevention*, 43(2), 498–515. <https://doi.org/10.1016/j.aap.2009.11.011>
- Worden, M. S., Foxe, J. J., Wang, N., & Simpson, G. V. (2000). Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 20(6), RC63. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10704517>
- Wright, K. P., & Badia, P. (1999). Effects of menstrual cycle phase and oral contraceptives on alertness, cognitive performance, and circadian rhythms during sleep deprivation. *Behavioural Brain Research*, 103(2), 185–194. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10513586>
- Wright, K. P., Hull, J. T., & Czeisler, C. A. (2002). Relationship between alertness, performance, and body temperature in humans. *American Journal of*

Physiology. Regulatory, Integrative and Comparative Physiology, 283(6), R1370-7. <https://doi.org/10.1152/ajpregu.00205.2002>

Yang, L., Hasher, L., & Wilson, D. E. (2007). Synchrony effects in automatic and controlled retrieval. *Psychonomic Bulletin & Review*, 14(1), 51–56. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17468781>

Yordanova, J., Kolev, V., & Polich, J. (2001). P300 and alpha event-related desynchronization (ERD). *Psychophysiology*, 38(1), 143–152. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11321615>

Yordanova, J., Kolev, V., Rosso, O. A., Schürmann, M., Sakowitz, O. W., Ozgören, M., & Basar, E. (2002). Wavelet entropy analysis of event-related potentials indicates modality-independent theta dominance. *Journal of Neuroscience Methods*, 117(1), 99–109. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12084569>

Zhu, Y., Xi, Y., Fei, N., Liu, Y., Zhang, X., Liu, L., ... Qin, W. (2018). Dynamics of cerebral responses to sustained attention performance during one night of sleep deprivation. *Journal of Sleep Research*, 27(2), 184–196. <https://doi.org/10.1111/jsr.12582>