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DEPARTAMENTO DE PSICOLOGÍA

TESIS DOCTORAL

EXCESO DE PESO EN ADOLESCENTES: INFLUENCIA DEL ESTRÉS SOCIAL EN EL RENDIMIENTO NEUROPSICOLÓGICO Y EFECTO DE LA VISUALIZACIÓN DE IMÁGENES DE ALIMENTOS EN LA ACTIVACIÓN CEREBRAL Y TOMA DE RIESGOS

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“Soy de las que piensan que la ciencia tiene una gran belleza. Un científico en su laboratorio no es sólo un técnico: también es un niño colocado ante fenómenos naturales que lo impresionan como un cuento de hadas”

(Marie Curie)

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Garantizan que:

La Tesis Doctoral titulada: "Exceso de peso en adolescentes: influencia del estrés social en el rendimiento neuropsicológico y efecto de la visualización de imágenes de alimentos en la activación cerebral y toma de riesgos.", realizada por la doctoranda María Moreno Padilla, ha sido elaborada bajo nuestra dirección y reúne las condiciones de calidad, originalidad y rigor científico necesarias para que se proceda a su defensa pública de acuerdo con la legislación vigente.

Fdo. Gustavo. A Reyes del Paso 

Fdo. María José Fernández Serrano 

Fdo. Antonio Verdejo García 

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Caminante, son tus huellas
el camino y nada más;
Caminante, no hay camino,
se hace camino al andar.
Al andar se hace el camino,
y al volver la vista atrás
se ve la senda que nunca
se ha de volver a pisar.
Caminante no hay camino
sino estelas en la mar

Decía Machado que solo se hace camino al andar, y así es. Yo, hace cuatro años, decidí escoger y caminar este sendero y, mirando atrás, contemplo mis huellas y pienso en lo mucho que se aprende, al andar, sobre los pasos que volverás y los que no volverás a dar. Porque al final el aprendizaje es precisamente eso, equivocarte, volver un poco atrás en el camino, aprender y seguir adelante. Al final, como decía Machado, son nuestras decisiones las que van construyendo nuestro propio sendero.

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Resumen

El aumento en la prevalencia de la obesidad se ha convertido en las últimas décadas, según la Organización Mundial de la Salud, en uno de los principales problemas de salud pública a nivel mundial. La obesidad es una condición compleja en la que intervienen multitud de factores.

En la antigüedad, las personas regulaban su ingesta según sus estados metabólicos de hambre y saciedad, sin embargo, en las sociedades occidentales actuales qué y cuánto comer se ha convertido en una cuestión de toma de decisiones. Estudios recientes apuntan a que el cambio en el estilo de vida actual, basado en el sedentarismo y hábitos alimenticios no saludables, es el responsable del drástico aumento de la prevalencia de la obesidad.

El exceso de peso y la obesidad también han aumentado exponencialmente en la infancia y la adolescencia, etapas críticas en el desarrollo del individuo. La adolescencia es una etapa en la que el individuo es especialmente vulnerable debido a sus peculiaridades comportamentales. En esta etapa son frecuentes los comportamientos dirigidos a la búsqueda de recompensa y propensión al riesgo, así como una disminución del control ejecutivo y la capacidad de regulación efectiva del comportamiento. En este sentido, distintos estudios confirman la existencia de alteraciones en el funcionamiento ejecutivo en adolescentes con exceso de peso comparados con adolescentes con peso saludable. Las funciones ejecutivas permiten una mejor regulación del comportamiento, y específicamente, del comportamiento alimenticio.

Por otro lado, el exceso de peso en la adolescencia no solo provoca consecuencias negativas a nivel de salud (diabetes tipo II, mayor probabilidad de desarrollar obesidad en la edad adulta y sus perjudiciales consecuencias médicas, etc.) sino que también está

asociado a un incremento del estrés social debido fundamentalmente a las frecuentes burlas que reciben por parte de sus iguales referidas a su imagen corporal y que, incluso, pueden llevar a la marginalización y exclusión social. Por tanto, los adolescentes con exceso de peso sufren mayor estrés social en su día a día. Numerosos estudios señalan el efecto perjudicial que produce el estrés en el rendimiento cognitivo. Así mismo, el estrés también puede alterar los patrones de alimentación a través de diversos mecanismos.

Como hemos comentado anteriormente, los mecanismos homeostáticos han quedado en segundo lugar para explicar el comportamiento alimenticio, siendo los procesos de toma de decisiones extremadamente importantes en esta cuestión. En concreto, el comportamiento impulsivo puede jugar un importante papel en la obesidad durante la infancia y la adolescencia. Distintos estudios han mostrado que la visualización de señales relacionadas con el consumo de drogas produce un incremento en los niveles de impulsividad e induce a una mayor toma de riesgos, incrementando como consecuencia el riesgo de consumo en individuos adictos a sustancias. Asimismo, varios estudios demuestran que las personas con exceso de peso tienen un sesgo atencional y mayor reactividad hacia señales de alimentos altos en grasas y/o azúcares.

Por otra parte, en los últimos años distintas investigaciones subrayan la superposición de las vías neurobiológicas implicadas en la adicción a sustancias y en la obesidad derivando en la creación del concepto “adicción a la comida”. Las drogas de abuso utilizan los mismos mecanismos neurales que modulan la motivación para consumir alimentos, por lo tanto, existe un paralelismo entre los circuitos cerebrales implicados en la pérdida de control y la ingesta excesiva de alimentos que caracteriza la obesidad y el consumo compulsivo de drogas propio de la adicción. La alteración de los circuitos cerebrales de dopamina es central en estas dos patologías. Concretamente, el sistema de

recompensa cerebral es un componente central para desarrollar y monitorear comportamientos motivados. Por lo tanto, el conocimiento de su funcionamiento es vital para comprender mejor el problema de la obesidad. Ante la visualización de alimentos altamente apetecibles o de gran aporte energético, las áreas del circuito de la recompensa pueden promover una mayor liberación de dopamina debido a la gran saliencia que tiene el estímulo y conllevar así a una mayor predisposición a la sobreingesta, al igual que sucede en estudios con poblaciones adictas a sustancias. En general, los resultados de los estudios de neuroimagen realizados hasta ahora señalan una respuesta incrementada en áreas del circuito de la recompensa, tanto en adultos como en adolescentes con exceso de peso, al procesar imágenes de comida, especialmente aquellas con un alto contenido en grasas y azúcares.

Tomando en consideración todo lo expuesto, los objetivos de esta tesis doctoral fueron: 1) estudiar la influencia del estrés social sobre el rendimiento neuropsicológico, en adolescentes con exceso de peso y adolescentes con normopeso, 2) analizar la influencia de la visualización de alimentos en una tarea de toma de decisiones de riesgo y su relación con la impulsividad, en adolescentes con exceso de peso comparados con adolescentes con normopeso, y 3) analizar el procesamiento cerebral durante las elecciones alimenticias y su relación con el *craving* subjetivo, en adolescentes con exceso de peso y adolescentes con normopeso.

Para abordar estos objetivos se llevaron a cabo 4 estudios. Los resultados obtenidos mostraron: 1) el estrés social se asocia con un peor rendimiento atencional y ejecutivo en adolescentes con exceso de peso, experimentando estos mayor reactividad autonómica ante ese estrés, con respecto a los adolescentes con normopeso (estudio 1 y 2); 2) los adolescentes con exceso de peso toman decisiones más arriesgadas tras la visualización de señales de alimentos y presentan mayores niveles de impulsividad que

los adolescentes con normopeso (estudio 3); y 3) se produce mayor activación de áreas cerebrales relacionadas con el circuito de la recompensa en el grupo de adolescentes con exceso de peso y observamos una asociación de la activación en estas áreas con el *craving* informado por los participantes hacia los alimentos presentados en la tarea (estudio 4).

Estos resultados podrían resultar de enorme utilidad tanto a nivel teórico, contribuyendo al avance del conocimiento de los factores que están predisponiendo al aumento de peso en la adolescencia, como a nivel clínico, impulsando nuevos tratamientos que tengan en cuenta variables neuropsicológicas y emocionales que contribuyan a mejorar las intervenciones pediátricas dirigidas a reducir los problemas de exceso de peso.

I. INTRODUCCIÓN

Capítulo 1

Obesidad

1. Definición y datos epidemiológicos

La Organización Mundial de la Salud (OMS) define la obesidad como una acumulación anormal y excesiva de grasa que puede ser perjudicial para la salud del individuo que lo padece. Tradicionalmente, instituciones como la OMS o la WOF ("World Obesity Federation" [anteriormente, International Obesity Task Force, (IOTF)], recomiendan utilizar el Índice de Masa Corporal (IMC) como medida de estimación del sobrepeso y la obesidad en los estudios de población (Pérez-Rodrigo, Bartrina, Majem, Moreno y Rubio, 2006). Este índice se calcula dividiendo el peso, en kilogramos, entre el cuadrado de la altura, en metros (kg/m^2). Para adultos, la OMS definió los umbrales indicando que un IMC mayor a 25 kg/m^2 está asociado a sobrepeso, y un IMC superior a 30 kg/m^2 a obesidad. En la edad adulta, estos puntos de corte están bien establecidos ya que, parece ser, que en esta etapa el IMC tiene una alta asociación con la grasa corporal o adiposidad, y también con las complicaciones clínicas derivadas de ésta (Flegal y Ogden, 2011). Sin embargo, en el caso de niños y adolescentes la determinación del IMC es más complicada ya que está asociado de forma más indirecta con el grado de adiposidad (Rolland-Cachera, 2011). La clasificación de la obesidad en la niñez y adolescencia se realiza siguiendo las indicaciones del IOTF (Cole, Bellizzi, Flegal y Dietz, 2000), las cuáles sugieren utilizar valores de IMC ajustados por edad (2-18 años) y sexo. Según esta clasificación, valores de percentil mayores de 85 se asocian a sobrepeso, mientras que se considera obesidad si estos valores superan el percentil 95.

Según la OMS, el aumento de la prevalencia de la obesidad se ha convertido en las últimas décadas en uno de los principales problemas de salud pública a nivel mundial. La prevalencia mundial de la obesidad casi se duplicó en el período comprendido entre 1980 y 2008, afectando en 2008 a quinientos millones de hombres y mujeres mayores

de 20 años, siendo más frecuente en las mujeres que en los hombres. Según este organismo, en 2014, más de 1900 millones de adultos de 18 ó más años tenían sobrepeso, de los cuales, más de 600 millones eran obesos, mientras que 41 millones de niños menores de cinco años tenían sobrepeso o eran obesos (OMS).

Por su parte, la WOF informa que si se mantiene la tendencia actual se calcula que en 2025 cerca de 2.700 millones de adultos tendrán sobrepeso, más de 1.000 millones tendrán obesidad y 177 millones de adultos sufrirán gravemente las consecuencias de ésta. La última evaluación del Instituto Médico Europeo de la Obesidad en 2014 indicó que, para esa fecha, el 21,1% de los niños españoles presentaban sobrepeso y el 8,2% presentaban obesidad, con lo que casi uno de cada tres niños de entre 3 y 12 años tenía exceso de peso. Datos del Centro Nacional de Investigaciones Cardiológicas indican que el porcentaje de la obesidad infantil ha aumentado un 35% en la última década. En esta misma línea, el informe de la Organización para la Cooperación y el Desarrollo Económicos (OCDE), en Estados Unidos y Gran Bretaña, indica que el 40% de la población infantil padece de obesidad. España es el segundo país de la Unión Europea, detrás de Gran Bretaña, con mayor porcentaje de niños obesos o con sobrepeso entre los 7 y los 11 años. De este modo, la obesidad se ha convertido en una epidemia que afecta cada año a 400.000 niños en todo el mundo (WOF, 2018).

2. Factores predisponentes y relevancia clínica del problema

Dada la alta prevalencia del sobrepeso y la obesidad en la adolescencia y el aumento de la severidad de esta, resulta de vital importancia conocer cuáles son los factores específicos que están causando o manteniendo dicha situación y qué consecuencias conlleva el exceso de peso en esta etapa.

La obesidad es una condición compleja en la que no solo influyen procesos metabólicos como el ingreso y gasto calórico. Los factores que pueden desencadenar la obesidad, son numerosos y de diversa índole, incluyendo factores genéticos, endocrinos, psicológicos y socioculturales. En cuanto al factor genético, aunque la ciencia ha demostrado que los genes pueden predisponer al sobrepeso (Locke y cols., 2015), este solo se produce cuando se combinan con otros factores, como los hábitos alimenticios y el estilo de vida (Martínez-Gómez y cols., 2011). De hecho, la genética por sí sola no puede explicar el rápido aumento de la obesidad en distintos países del mundo. Por otro lado, existen algunas alteraciones de la función endocrina que pueden provocar la obesidad, como el síndrome de Cushing (una enfermedad provocada por el aumento de la hormona cortisol), alteraciones en la tiroides, o el hipogonadismo (Wierman, 2003). En cuanto a los factores socioculturales, el aumento del sedentarismo, el cambio en los patrones de sueño, así como la total disponibilidad que tenemos de alimentos altamente calóricos a precios asequibles en las sociedades occidentales actuales (Sahoo y cols., 2015; Ellulu, Abed, Rahmat, Ranneh y Ali, 2014), son variables a tener en cuenta a la hora de abordar el problema del aumento de prevalencia de la obesidad. El sedentarismo afecta a adultos (mayor uso de transportes, ascensores, escaleras mecánicas, tiempo dedicado a la televisión, etc.), pero también a niños y adolescentes, los cuales pasan mucho tiempo sentados, ya sea mirando televisión o utilizando dispositivos electrónicos, como las consolas de videojuegos, los ordenadores portátiles o los *smartphones*. Esto provoca que el gasto energético sea bajo y que resulte difícil deshacerse de las calorías consumidas. Por otro lado, el sueño deficiente es cada vez más común en los niños y las asociaciones entre la corta duración del sueño en la primera infancia y la obesidad se encuentran consistentemente a través de la literatura (Hasler y cols., 2004; Cappuccio y cols., 2008; Miller, Lumeng & LeBourgeois, 2015).

Los factores psicológicos también son de vital importancia a la hora de entender la obesidad. En ocasiones, las personas recurren a la comida cuando se encuentran bajo estados emocionales negativos (estrés, tristeza, enfado, frustración, soledad, etc.) como una forma de liberar su ansiedad (Faith, Allison & Geliebter, 1997).

Todos los factores anteriormente mencionados confluyen a la hora de crear una determinada predisposición a desarrollar obesidad. Además, algunos estudios indican que los drásticos cambios producidos en el entorno y el estilo de vida han modificado la forma en la que percibimos los alimentos y regulamos su ingesta (Zheng, Lenard, Shin y Berthoud, 2009). Nuestros antepasados comían para asegurar la supervivencia, ellos se guiaban solamente por sus sistemas de regulación metabólica (hambre y saciedad). Sin embargo, actualmente, qué y cuánto comer se ha convertido en una cuestión de toma de decisiones, otorgamos a la comida un valor hedónico similar al que otorgamos a otras actividades reforzantes (Zheng y cols., 2009). Además, diversos estudios han encontrado que los alimentos altamente apetitosos (altos en grasas y/o azúcares) activan regiones del área de recompensa cerebral, al igual que hacen las drogas de abuso, lo que conlleva que este tipo de alimentos tengan un valor hedónico y reforzante similar, pudiendo llegar a convertirse en un comportamiento abusivo y compulsivo (Volkow, Wang, Fawler y Telang, 2008; Volow, Wang, Fowler, Tomasi, Baler, 2011; Volkow, Wang, Tomasi y Baler, 2013).

En cuanto a las consecuencias del exceso de peso en la adolescencia, la obesidad se relaciona con un mayor número de complicaciones médicas directas (tolerancia a la glucosa, diabetes tipo 2) e indirectas (absentismo escolar, visitas al médico), además de mayor riesgo cardiovascular en la edad adulta y los costes sociales que no pueden ser directamente estimados (Lobstein, Baur y Uauy, 2004; Baker, Olsen, Sorensen, 2007; DeBoer, 2013; Goran, Ball y Cruz, 2003).

En concreto, la diabetes tipo 2, conocida hasta hace poco tiempo como diabetes del adulto, ya que prácticamente sólo aparecía en la edad adulta, ha aumentado de forma significativa entre niños y adolescentes de todo el mundo en los últimos 15 años. La diabetes está estrechamente relacionada con el exceso de peso, por lo tanto, la causa de este aumento parece ser el incesante crecimiento de la obesidad infantil (DeBoer, 2013; Goran y cols., 2003). El aumento de peso, los hábitos alimenticios no saludables y la falta de actividad física provocan un mal funcionamiento de la insulina causando una alteración denominada "resistencia a la insulina". Al principio, el cuerpo compensa este déficit aumentando la producción de insulina. Sin embargo, con el tiempo y debido a que cada vez se consumen más alimentos ricos en azúcares y harinas refinadas, la capacidad del páncreas para incrementar la producción no se mantiene y el azúcar/glucosa en sangre empieza a aumentar, provocando finalmente una diabetes tipo 2.

También, existe evidencia de que el exceso de peso es un factor de riesgo para desarrollar problemas de ajuste social en la adolescencia (Puhl y Heuer, 2009), así como problemas de baja autoestima, estigmatización y síntomas depresivos (Chaiton y cols., 2009). Por tanto, los adolescentes con exceso de peso sufren de más estrés social que sus compañeros con normopeso. De este modo, la evaluación de los posibles efectos que el estrés social pueda estar causando en el procesamiento cognitivo y la toma de decisiones de los adolescentes con exceso de peso son de vital importancia a la hora de tener un conocimiento más certero acerca de las causas que puedan estar desarrollando y manteniendo el problema de la obesidad. Este es un tema que desarrollaremos más profundamente en el capítulo 3.

Por otro lado, diversos estudios y revisiones recientes confirman que el exceso de peso en la infancia y adolescencia es un fuerte factor predisponente para el desarrollo de la

obesidad en la edad adulta (Guo, Wu, Chumlea y Roche, 2002; Singh, Mulder, Twisk, Van Mechelen y Chinapaw, 2008). Según la OMS, un IMC elevado en la edad adulta es un importante factor de riesgo para desarrollar enfermedades cardiovasculares (que fueron la principal causa de muerte en 2012), diabetes, trastornos del aparato locomotor (en especial, osteoartritis) y algunos tipos de cánceres. Los costes médicos asociados a la obesidad en la edad adulta parecen superar a los provocados por el consumo de tabaco o alcohol (Sturm, 2002).

En resumen, padecer obesidad predispone al desarrollo de múltiples problemas de salud y de ajuste social en el individuo. Estos problemas resultan aún más significativos si la obesidad ocurre en la adolescencia.

Capítulo 2

Rendimiento neuropsicológico, toma de riesgos e impulsividad en la obesidad

1. Rendimiento neuropsicológico

En los últimos años distintas investigaciones subrayan la superposición de las vías neurobiológicas implicadas en la adicción a sustancias y en la obesidad, derivando en la creación del concepto "adicción a la comida" (Volkow, Wang, Fawler y Telang, 2008; Volow, Wang, Fowler, Tomasi, Baler, 2011; Volkow, Wang, Tomasi y Baler, 2013). En ambas condiciones, la evaluación de la motivación por el estímulo elegido (drogas o alimentos apetecibles) está exageradamente exaltada, mientras que el sistema de control "top-down" que normalmente regula las respuestas guiadas por las recompensas está alterado (Acosta, Manubay y Levin, 2008). Esta interacción anormal entre la regulación de la motivación homeostática y el control del comportamiento ha sido relacionada con alteraciones en las funciones ejecutivas (Berthoud, 2007).

Las funciones ejecutivas son un conjunto de habilidades implicadas en la generación, la supervisión, la regulación, la ejecución y el reajuste de conductas adecuadas para alcanzar objetivos complejos, especialmente aquellos que requieren un abordaje novedoso y creativo (Gilbert y Burgess, 2008; Verdejo-García y Bechara, 2010). Se trata de habilidades esenciales para nuestro día a día ya que se ponen en marcha en una amplísima variedad de situaciones y su correcta competencia es vital para un funcionamiento óptimo y socialmente adaptado. Las funciones ejecutivas se componen tanto de recursos atencionales como de recursos mnésicos, pero su función es la de proporcionar un espacio operativo y un contexto de integración de estos procesos con objeto de optimizar la ejecución en función del contexto actual (externo, interoceptivo y metacognitivo) y de la previsión de nuestros objetivos futuros (Verdejo-Barcía y Bechara, 2010). Estas funciones, muestran importantes deterioros en pacientes con lesiones que afectan a la corteza frontal (Stuss y Levine, 2002), lo que ha llevado a

considerar esta región como el principal sustrato neuroanatómico de estas habilidades, razón por la cual en la adolescencia estas funciones están más limitadas que en la edad adulta ya que el córtex prefrontal (PFC) no ha completado su maduración a esta edad. Las funciones ejecutivas se dividen en cuatro componentes (Verdejo-García y Pérez-García, 2007): actualización (formado a su vez por memoria de trabajo, razonamiento y fluidez), control inhibitorio, flexibilidad cognitiva y toma de decisiones. El componente de actualización implica la monitorización, actualización y manipulación de la información "*on line*" en la memoria operativa. El control inhibitorio se refiere a la capacidad para cancelar respuestas automatizadas, impulsivas o guiadas por la recompensa que son inapropiadas para las demandas actuales. Se trata de un constructo multidimensional asociado con distintos procesos neuropsicológicos con bases cerebrales relativamente independientes: inhibición de respuestas, autorregulación, entre otros. La flexibilidad cognitiva o "shifting" es la capacidad de reestructurar el propio conocimiento de forma espontánea para dar una respuesta adaptada a las exigencias cambiantes del ambiente. Por último, la toma de decisiones es la habilidad para seleccionar de entre un conjunto de posibles alternativas existentes aquella que resulta más adaptativa para el individuo (Verdejo-García y Bechara, 2010).

La alteración en las funciones ejecutivas puede ser mayor en la adolescencia, ya que se trata de un periodo caracterizado por la inmadurez relativa de los sistemas de control prefrontales, a su vez unido con la madurez de los sistemas subcorticales responsables de la motivación y el procesamiento de la recompensa (Chambers, Taylor y Potenza, 2003). Por un lado, estudios con resonancia magnética funcional (fMRI) han señalado que los adolescentes, comparados con los adultos, muestran mayor activación del estriado ventral y de la ínsula anterior durante la anticipación de la recompensa y su consecución (Van Leijenhorst y cols., 2009; Ernst y cols., 2005). Por otro lado, los

resultados de estudios cognitivos que han empleado fMRI, han mostrado que las habilidades de control ejecutivo y sus sustratos neurales (p.ej. PFC) están todavía mejorando su competencia durante la adolescencia temprana y tardía (Bunge y Wright, 2007; Waber y cols., 2007; Crone, Bullens, van der Plas, Kijkuit y Zelazo, 2008). Este desequilibrio hace que la adolescencia sea un período durante el cual la actividad del sistema de recompensa prevalece sobre la de los sistemas que gobiernan la evitación de daños y el autocontrol (Chambers y cols., 2003). Por lo tanto, los sistemas encargados del funcionamiento ejecutivo son sumamente importantes en esta etapa.

Respecto a la obesidad y el funcionamiento ejecutivo, distintos estudios confirman la existencia de alteraciones en este funcionamiento en adolescentes con exceso de peso comparados con adolescentes con peso saludable. Varios estudios (Kamijo, Khan y cols., 2012; Kamijo, Pontifex, y cols., 2012) han mostrado una correlación negativa del IMC con el rendimiento en control cognitivo en un grupo de pre-adolescentes con obesidad. Respecto al componente de inhibición, un estudio de Anzman y Birch (2009) señaló que los participantes con bajo control inhibitorio a los 7 años tendían a tener un IMC mayor a los 15 años. Riggs, Huh, Chou, Spruijt-Metz y Pentz (2012) y Riggs, Spruijt-Metz, Chou y Petz (2012) señalaron que los niños altamente sedentarios que no eran conscientes de su peso y consumían alimentos altos en grasas y/o azúcares mostraban menor control inhibitorio que los niños activos que consumían frutas y verduras. Asimismo, distintos estudios han señalado que los adolescentes con obesidad muestran peor control inhibitorio y, por lo tanto, peor rendimiento en tareas go/no go y de retraso de la recompensa (tareas “delay-discounting”) que el grupo con peso saludable (Pauli-Pott, Albayrak, Hebebrand y Pott, 2010; Bruce, Martin y Savage, 2011). Respecto a la memoria de trabajo (el componente de actualización más estudiado), Riggs, Huh y cols (2012) y Riggs, Spruijt-Metz y cols (2012) también

señalaron una correlación negativa entre el sedentarismo y el consumo de alimentos altos en grasas y/o azúcares y el rendimiento en este componente. Por otro lado, Maayan, Hoogendoorn, Sweat y Convit (2011) también encontraron que los adolescentes con obesidad rendían peor en tareas de memoria de trabajo [*Wide Range Assessment of Learning and Memory* (WRAML)] que los adolescentes con peso saludable. En lo relacionado con la flexibilidad cognitiva, hay estudios que muestran que los adolescentes con exceso de peso muestran peor rendimiento en este componente en una variedad de tareas utilizadas (Trail Making Test, Test de Cartas de Wisconsin, condición de cambio en el Test de los Cinco Dígitos, etc.) (Verdejo-García y cols., 2010; Lokken, Boeka, Austin, Gunstad y Harmon, 2009; Cserjési, Molnár, Luminet y Lénárd, 2007; Delgado-Rico, Río-Valle, González-Jiménez, Campoy y Verdejo-García, 2012). Por último, Verdejo-García y cols. (2010) utilizaron la Iowa Gambling Task (IGT) para evaluar toma de decisiones y observaron que los adolescentes con sobrepeso presentaban un rendimiento significativamente menor que los adolescentes con normopeso.

En resumen, la evidencia científica existente revela de forma consistente una asociación inversa entre la obesidad y las funciones ejecutivas en niños y adolescentes. Sin embargo, es imperativo determinar la dirección de esta asociación, así como unificar el método de evaluación de las funciones ejecutivas. En concreto, aún se desconoce si los déficits cognitivos son anteriores al desarrollo de la obesidad (y, por tanto, pudieran actuar como factor de vulnerabilidad) o si es una consecuencia de esta condición. Así mismo, la variedad de instrumentos y procedimientos utilizados a través de los estudios hacen difícil la generalización de resultados.

2. Toma de riesgos e impulsividad

Identificar estilos de comportamiento específicos asociados con la obesidad representa un paso importante para mejorar potencialmente los métodos de prevención y tratamiento. En nuestra sociedad actual, llena de alimentos altos en grasas y/o azúcares totalmente disponibles, el autocontrol es necesario para evitar la sobre ingesta. Por lo tanto, los mecanismos homeostáticos han quedado en segundo lugar para explicar el comportamiento alimenticio, siendo los procesos de toma de decisiones extremadamente importantes en esta cuestión. En concreto, el comportamiento impulsivo puede jugar un importante papel en la obesidad durante la infancia y la adolescencia.

La impulsividad describe la tendencia a actuar con menos previsión, y predispone a un individuo a reacciones precipitadas, no planificadas, sin tener en cuenta las consecuencias negativas y obviando las elecciones racionales a largo plazo. La impulsividad es considerada un conjunto multidimensional que engloba múltiples características. Uno de los instrumentos de autoinforme más utilizados para evaluar impulsividad es el cuestionario UPPS-P (Verdejo-García, Lozano, Moya, Alcázar, Pérez-García, 2010). El modelo que sigue este cuestionario identifica cuatro vías diferentes que conducen al comportamiento impulsivo: urgencia (positiva y negativa), falta de premeditación, falta de perseverancia y búsqueda de sensaciones. La urgencia positiva se refiere a la tendencia a experimentar fuertes impulsos y falta de control inhibitorio cuando la persona se encuentra bajo estados de ánimos positivos; mientras que la urgencia negativa implica el aumento de la impulsividad y la falta de inhibición bajo condiciones de afecto negativo. La falta de premeditación se refiere a la tendencia a pensar y reflexionar sobre las consecuencias de un acto antes de participar en ese acto o tomar una decisión. La falta de perseverancia se refiere a la capacidad de permanecer

enfocado en una tarea que puede ser larga, aburrida o difícil. Finalmente, la búsqueda de sensaciones abarca dos aspectos: (a) la tendencia a disfrutar y llevar a cabo actividades emocionantes y (b) una apertura a probar nuevas experiencias que pueden o no ser peligrosas. La puntuación en búsqueda de sensaciones se correlaciona positivamente con sensibilidad a la recompensa porque ambas dimensiones se relacionan con el inicio del comportamiento de aproximación asociado con la novedad o con la perspectiva de recompensa (Verdejo-García y cols., 2010).

La impulsividad se ha relacionado tradicionalmente con varias conductas de alto riesgo en los jóvenes, como el consumo de sustancias (p. ej. cigarrillos, alcohol), el juego, la agresión y el comportamiento sexual de alto riesgo (Steinberg, 2004; Miller, Naimi, Brewer y Jones, 2007). Además, la impulsividad hace que sea más difícil resistir la tentación de comer alimentos apetecibles normalmente altos en calorías y, por lo tanto, puede contribuir al exceso de peso. Existe cierta evidencia de que las personas con obesidad son más propensas a ceder ante las tentaciones y son menos efectivas para inhibir sus impulsos. Estudios con medidas de autoinforme muestran que las personas con obesidad son más impulsivas que las personas con normopeso y muestran comorbilidad con otras conductas impulsivas, como el abuso de sustancias (Rydén y cols., 2003). Además, se ha encontrado que los niños obesos son menos capaces de retrasar la gratificación y, más a menudo, eligen una recompensa inmediata sobre una recompensa retrasada más grande, siendo este un índice de poco auto-control (Bonato y Boland, 1983; Best et al., 2012). Investigaciones recientes también han demostrado que los niños y adolescentes con obesidad son menos efectivos en la inhibición de respuesta en una tarea “stop-signal”, son más sensibles a la recompensa y toman más riesgos en una variedad de tareas de toma de decisiones, asociándose un mayor peso a un

comportamiento más impulsivo (Nederkoorn, Braet, Van Eijs, Tanghe y Jansen, 2006; Thamotharan, Lange, Zale, Huffhines y Fields, 2013; Davis, Patte, Curtis y Reid, 2010).

Las habilidades de toma de decisiones son particularmente relevantes en el caso de los adolescentes, en quienes las transiciones cerebrales del desarrollo parecen estar programadas para maximizar la recompensa a expensas del riesgo. Relacionado con esto, aparece el concepto de toma de riesgos, asociado a características impulsivas y de toma de decisiones y que ha sido ampliamente estudiado en comportamientos adictivos.

La toma de riesgos describe la tendencia a participar en un comportamiento que tiene una probabilidad relativamente alta de un resultado negativo y está asociado con el abuso de sustancias (Lejuez, Bornovalova, Daughters y Curtin, 2005), desórdenes alimenticios (Boeka y Lokken, 2006), y comportamientos sexuales de riesgo (Lawyer, 2013). El exceso de peso también se asocia con la toma de riesgos ya que los participantes con obesidad muestran patrones de toma de decisiones más arriesgadas en la tarea IGT (Bechara, 2007), una medida usual de toma de riesgos (Boeka y Lokken, 2006; Brogan, Hevey y Pignatti, 2010). Estudios de neuroimagen también han demostrado que los adolescentes con exceso de peso tienen una respuesta estriatal hipersensible (Cohen y cols., 2010; Galvan y cols., 2006) y una activación aumentada en regiones cerebrales envueltas en el fomento de la toma de riesgos [córtex orbitofrontal (OFC)] durante la toma de decisiones (Van Leijenhorst y cols., 2009).

Una tarea ampliamente utilizada para evaluar toma de riesgos es la Balloon Analogue Risk Task (BART) (Lejuez y cols., 2002). En esta tarea, los participantes acumulan dinero en un banco temporal presionando un botón que infla un globo simulado. Cada globo tiene un punto de explosión (desconocido por el participante) que, si se alcanza, da como resultado la pérdida de todo el dinero en el banco temporal. Antes de la

explosión de cada globo, los participantes tienen la opción de presionar un botón de guardar que transferirá su dinero a un banco permanente. Hay un número determinado de globos, e independientemente de si el globo explota o se si se guarda el dinero acumulado, el participante pasa al siguiente globo. Por lo tanto, el participante debe equilibrar la ganancia potencial de acumular más dinero con el riesgo potencial de perder todo el dinero acumulado en ese globo. A diferencia de la tarea IGT, tarea muy utilizada para la evaluación de la toma de decisiones, en la que cada prueba implica una elección entre una alternativa de riesgo y otra segura (mediante selección de cartas), la BART implica un número variable de elecciones en un contexto de riesgo creciente (es decir, la cantidad de dinero acumulado y la probabilidad de perder ese dinero aumenta cada vez que se infla el globo). El riesgo en esta tarea está asociado con la ocurrencia de conductas de riesgo en el mundo real (Lejuez, Aklin, Zvolensky y Pedulla, 2003). En concreto, la puntuación en la BART se considera una medida de las diferencias individuales en la propensión a tomar decisiones arriesgadas, y se ha encontrado que las puntuaciones altas en BART se relacionan con la asunción de riesgos en la adolescencia (Lejuez, Aklin, Zvolensky y cols., 2003), el tabaquismo (Lejuez, Aklin, Jones y cols., 2003) y el abuso de drogas (Hopko y cols., 2006).

Por otra parte, la literatura muestra que distintos contextos o elementos como, por ejemplo, la visualización de señales relacionadas con el comportamiento abusivo, pueden exacerbar la tendencia impulsiva del individuo. En concreto, distintos estudios han mostrado que la visualización de señales relacionadas con el consumo de drogas produce un incremento en los niveles de impulsividad e induce a una mayor toma de riesgos, incrementando como consecuencia el riesgo de consumo en estos individuos (Field y Eastwood, 2005; Fox y cols., 2005). Asimismo, varios estudios demuestran que las personas con exceso de peso tienen un sesgo atencional hacia señales de alimentos

altos en grasas y/o azúcares (Hou y cols., 2011; Castellanos y cols., 2009). Por lo que parece razonable esperar que, del mismo modo que en los individuos adictos a sustancias, los adolescentes con exceso de peso asuman mayores riesgos al encontrarse en un contexto que favorezca la visualización de alimentos muy apetitosos.

Capítulo 3

Estrés social y obesidad

1. Estrés social en adolescentes con exceso de peso

El sobrepeso durante la adolescencia no solo tiene consecuencias a nivel de salud, sino que también tiene efectos nocivos en el ámbito social y psicológico. Padecer sobrepeso u obesidad en la niñez y adolescencia tiene unas consecuencias perjudiciales muy significativas en el desarrollo emocional y en el bienestar general del niño y adolescente (Strauss y Pollack, 2003). Numerosos estudios han encontrado que los adolescentes con exceso de peso tienen mayor probabilidad de desarrollar síntomas depresivos y además poseen menores niveles de autoestima que sus iguales con peso saludable. En este sentido, los estudios desarrollados por Richardson, Goodman, Hastorf y Dornbusch (1961) ya en la década de 1960 indicaban que los niños con sobrepeso eran considerados por los otros niños como los amigos menos deseables.

La amistad es un vehículo esencial para el ajuste psicológico y social de los adolescentes. Dadas las normas estrictas de apariencia entre los adolescentes en cuanto a imagen corporal, el sobrepeso puede tener importantes consecuencias sobre el desarrollo del niño y el bienestar del adolescente. En un estudio de Strauss y Pollack (2003) se comprobó que los adolescentes con exceso de peso sufrían mayor marginalización social y estigmatización, y este aislamiento agravaba las consecuencias sociales y emocionales del sobrepeso en este grupo de edad. Distintos estudios confirman que los estereotipos negativos hacia el sobrepeso empiezan en la infancia temprana (Cramer y Steinwert, 1998; Rich y cols., 2008), y la victimización de los adolescentes basada en su sobrepeso es muy común (Haines, Neumark-Sztainer, Hannan, van den Berg y Eisenberg, 2008). Es más probable que los adolescentes con exceso de peso y obesidad se conviertan en objeto de burlas y bullying que sus compañeros con normopeso (Janssen, Craig, Boyce y Pickett, 2004; Hayden-Wade y cols., 2005; Pearce, Boergers y Prinstein, 2002). La probabilidad de victimización

verbal, social y física entre los adolescentes aumenta con el IMC (Janssen y cols., 2004), además estudios longitudinales demuestran que el peso corporal predice significativamente la victimización futura (Griffiths, Wolke, Page, Horwood y Team, 2006), siendo los adolescentes con mayor nivel de obesidad especialmente vulnerables a la estigmatización y presión social. La literatura sugiere que un tercio de las chicas y un cuarto de los chicos reportan burlas basadas en el peso por sus compañeros, pero esta prevalencia aumenta hasta aproximadamente el 60% entre los estudiantes con mayor nivel de obesidad (Neumark-Sztainer y cols., 2002). En un estudio de Puhl, Luedicke y Heuer (2011) en el que utilizaron las valoraciones de los estudiantes con peso saludable, los resultados mostraron que los participantes percibían que el sobrepeso y la obesidad era la primera razón de sufrir acoso y estigmatización en la escuela.

Las personas con sobrepeso y obesas son altamente estigmatizadas en nuestra sociedad, y los estereotipos basados en el peso siguen siendo generalizados, incluyendo la percepción de que las personas obesas son perezosas, desmotivadas, incompetentes, descuidadas, carentes de autodisciplina y carentes de voluntad (Puhl y Brownell, 2001; Puhl y Heuer, 2009). Para los jóvenes que presentan sobrepeso u obesidad, la estigmatización del peso se traduce en victimización generalizada, burlas e intimidación. Estas experiencias pueden ser explícitas (p. ej. burlas verbales, insultos, violencia física), o pueden tomar formas más sutiles, como victimización relacional (p. ej. exclusión social, evitación, ser objeto de rumores).

En resumen, los niños con sobrepeso u obesidad son con frecuencia víctimas de burlas, acoso, discriminación y otras formas de marginación social. Por lo tanto, los adolescentes con exceso soportan un estrés social elevado.

Hay evidencia de las consecuencias emocionales negativas del estrés social en adolescentes con exceso de peso. Las burlas basadas en el peso pueden contribuir a consecuencias emocionales negativas para niños y adolescentes ya que aumenta el riesgo de depresión, ansiedad, baja autoestima e insatisfacción corporal (Puhl y Heuer, 2009; Eisenberg, Neumark-Sztainer y Story, 2003). La consecuencia emocional más dramática que ocurre entre los adolescentes que sufren marginalización por su peso es el aumento del riesgo de comportamiento suicidas (Eaton, Lowry, Brener, Galuska y Crosby, 2005).

Además de las consecuencias a nivel social en el ámbito escolar, las consecuencias perjudiciales a nivel académico también son frecuentes. La evidencia indica que los adolescentes que sufren de continuas burlas y acoso sufren mayor absentismo escolar, lo que perjudica su rendimiento académico (Puhl y Luedicke, 2012).

2. Influencia del estrés social sobre la conducta alimentaria

Muchos factores externos pueden influir en la ingesta de alimentos, entre los que se incluyen factores ambientales (p.ej. económicos, disponibilidad de alimentos) (Popkin, Duffey y Gordon-Larsen, 2005), factores sociales (p.ej. influencia de otros) y la palatabilidad de los alimentos, entendida como el valor hedónico que otorgamos a la comida y que depende de las propiedades organolépticas del alimento como, por ejemplo, su sabor, olor o apariencia (Pliner y Mann, 2004). Además de esto, es una creencia comúnmente sostenida que el estrés puede alterar los patrones de alimentación (Wardle y Gibson, 2002).

La salud física, y en concreto, el comportamiento alimenticio, también puede verse afectado por el estrés social que sufren las personas con sobrepeso y obesidad. Los mecanismos biológicos directos que vinculan el estrés con la obesidad implican la

elevación prolongada del cortisol circulante, un marcador de la activación hipotalámica del eje pituitario-adrenal, que puede aumentar el apetito y la deposición de grasa visceral (Bjorntorp, 2001) (ver Figura 1).

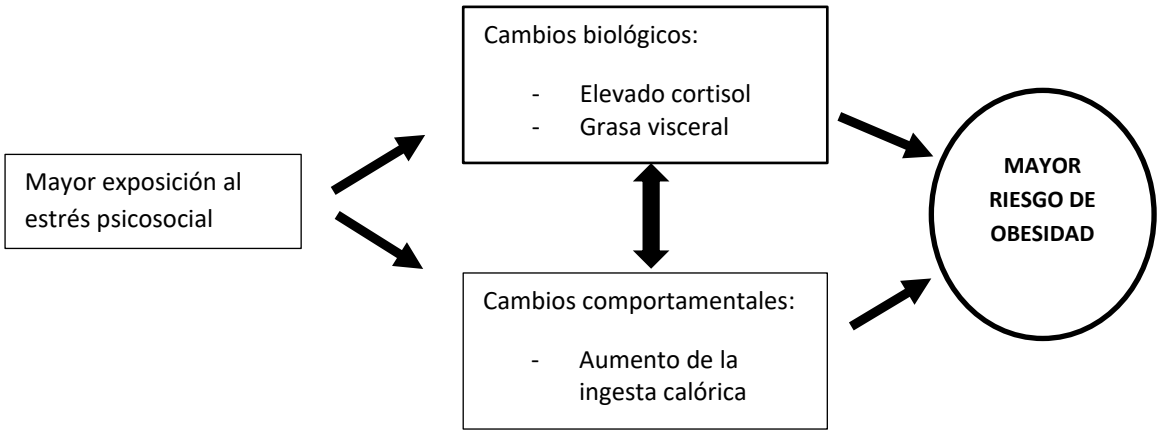


Figura 1. Vías a través de las cuales el estrés puede contribuir al desarrollo de la obesidad.

En humanos, la literatura muestra que el estrés influencia la conducta alimenticia de forma bidireccional; posiblemente alrededor del 30% de los individuos disminuye la ingesta de alimentos y pierde peso durante o después del estrés, mientras que la mayoría de las personas aumentan su ingesta durante el estrés (Stone y Brownell, 1994; Epel y cols., 2004). Teniendo en cuenta que las personas que viven en países occidentalizados viven en un entorno alimenticio apetecible, con una abundancia de alimentos calóricamente densos, tiene sentido que la mayoría de las personas refieran comer más durante la situación estresante, en lugar de comer menos. Casi el 50% de una muestra representativa de EE.UU. afirmó estar preocupada por la cantidad de estrés en sus vidas al ser conscientes de la relación entre este estrés y su involucración en comportamientos poco saludables como fumar y comer como forma de aliviarse de esas situaciones (Stambor, 2006). El deseo -inducido por el estrés- por alimentos altamente calóricos es alarmante teniendo en cuenta la creciente epidemia de obesidad.

Así mismo, se ha observado que las personas con exceso de peso presentan frecuentemente un patrón de ingesta emocional basado en la tendencia a consumir de manera impulsiva cuando están bajo un estado emocional negativo (ansiedad, depresión, estrés, etc.). Como hemos comentado, el estrés agudo puede aumentar la ingesta, especialmente cuando hay alimentos apetitosos (altos en calorías) disponibles (Oliver y Wardle, 1999; Bjorntorp, 2001). Por ejemplo, un estudio con autoinformes señaló que el 42% de los estudiantes informaban que incrementaban su ingesta después de percibir estrés, y el 73% de los participantes informaban incrementar el "picoteo" durante el estrés (Oliver y Wardle, 1999). En esta misma línea, un estudio de Jääskeläinen y cols. (2014) encontró que los adolescentes que se dejaban llevar por el estrés a la hora de comer tenían una mayor prevalencia de obesidad que los que no lo hacían. Otro estudio señaló que las mujeres que reportaban mayor estrés crónico también reportaban ser "comedoras emocionales" (Tomiyama, Dallman y Epel, 2011). Hay evidencia significativa que sugiere efectos potencialmente perjudiciales del estrés en los patrones de alimentación (p. ej. omitir las comidas, restringir la ingesta, atracones) y las preferencias alimentarias basadas en alimentos apetecibles altos en calorías (Torres y Nowson, 2007). Distintas investigaciones muestran que los efectos del estrés pueden ser diferentes en las personas con peso saludable en comparación con las personas con obesidad (Block, He, Zaslavsky, Ding y Ayanian, 2009; Lemmens, Rutters, Born y Westerterp-Plantenga, 2011; Jastreboff y cols., 2011). Se ha observado que la alimentación debida al estrés se exacerba en las personas con obesidad, mientras que la ingesta emocional parece tener un efecto inconsistente en individuos con normopeso (Laitinen, Ek y Sovio, 2002).

Los adolescentes con exceso de peso, los cuales hemos comentado que se encuentran bajo un estrés social recurrente, podrían utilizar la sobreingesta de alimentos altos en

grasas y/o azúcares como estrategia de afrontamiento a esa situación. Así, las funciones cognitivas superiores de control ejecutivo podrían estar alteradas tras estas situaciones emocionalmente negativas, facilitándose de esta manera, la dificultad para inhibir los impulsos ante la presencia de alimentos altamente calóricos en el ambiente (Dallman y colsy cols., 2003; Dallman, Pecoraro y la Fleur, 2005).

Por otro lado, el modelo "*Reward Based Stress Eating*" (Adam y Epel, 2007) enfatiza el papel del cortisol y los circuitos de recompensa en la motivación de la ingesta de alimentos altamente calóricos, y señala el papel de los mediadores neuroendocrinos en la relación entre el estrés y la alimentación. A nivel fisiológico, existe evidencia que sostiene que la ghrelina u "hormona del hambre" aumenta en respuesta de estresores sociales (p.ej. después de la Trier Social Stress Task, que se basa en un discurso público) (Rouach y cols., 2007) al igual que el cortisol u "hormona del estrés" que está asociado positivamente con la posterior ingesta de lípidos (Therrien y cols., 2007; Bjorntorp, 2001).

3. Reactividad psicofisiológica al estrés

Está ampliamente aceptado que el estrés psicológico puede producir reactividad fisiológica similar a la producida por desafíos de carácter físico. Existen tres sistemas primarios que están particularmente involucrados en el establecimiento de la respuesta al estrés, el sistema nervioso autónomo (SNA), el eje hipotálamo-hipófisis-adreno cortical (HHCA) y el simpático-adrenomedular (SAM). La activación del eje HHCA causa un aumento en la secreción de cortisol, un glucocorticoide liberado por la corteza suprarrenal, conocido como "la hormona del estrés" (Sapolsky, Krey y McEwen, 1986; Al'Absi y Arnett, 2000). La recogida de muestra de cortisol salival ha sido muy recurrente en investigaciones sobre estrés. Las concentraciones de cortisol salival están

estrechamente correlacionadas con la concentración de cortisol sérico o en plasma (Kirschbaum y Hellhammer, 1994. El cortisol salival es una herramienta de evaluación más práctica que la recolección de sangre, ya que este método refleja una tendencia a provocar aumentos espurios en la secreción de cortisol. Muchos informes han demostrado que diversos tipos de estrés psicológico activan la liberación de cortisol y, en consecuencia, inducen aumentos significativos en el nivel de cortisol salival (Kirschbaum y Hellhammer, 1994). La toma de muestras de saliva tiene la ventaja de que es un método no-invasivo, lo que hace que la recogida de muestras múltiple sea fácil y libre de estrés. La medida de cortisol ha sido utilizada como medida de la respuesta al estrés psicosocial en varias investigaciones (Kirschbaum y Hellhammer, 1994).

Por otro lado, además del cortisol, para evaluar la reactividad ante el estrés en una situación de laboratorio se puede recurrir a otras medidas fisiológicas de la actividad del SNA. Entre ellas, la frecuencia cardíaca (FC) y la actividad electrodermal (AED) han sido ampliamente utilizadas, ya que reflejan el grado de reactividad fisiológica que experimenta el sujeto al afrontar una situación estresante (Kuhmann, Boucsein, Schaefer y Alexander, 1987; Kohlish y Schaefer, 1996). La intensidad y el patrón de las respuestas de la FC y la AED ante situaciones de estrés dependen de las características del estresor, de los recursos psicosociales que posea el sujeto y de los factores biológicos y constitucionales del individuo, así como de la interacción entre estos componentes (Steptoe, 1990; Peters y cols., 1998). La FC se considera una variable muy sensible a los estresores (Freyschus, Hjemdahl, Juhlin-Dannfelt y Linde, 1988), aporta información de regulación autonómica del corazón, no es invasiva y se puede registrar de forma continua. La FC se incrementa normalmente en el laboratorio tras la utilización de diversos estresores como la tarea "Stroop" (Goldberg y cols., 1996),

hablar en público (Kirschbaum y cols., 1995; Carrillo, Moya-Albiol, González-Bono y Salvador, 2000; Verdejo-García y cols., 2015), tareas aritméticas (Sloan y cols., 1997), tareas de tiempo de reacción (Marrero, Al'Absi, Pincomb y Lovallo, 1997). La reactividad en FC ante un estresor psicológico en una situación de laboratorio puede ser utilizada como un indicador bastante fiable de la reactividad cardíaca en otras situaciones semejantes de laboratorio o de la vida real, ya que las variaciones en FC son los cambios cardiovasculares más estables en el tiempo (Swain y Suls, 1996). La AED ha sido uno de los índices psicofisiológicos más empleado como correlato de procesos psicológicos, ya que se ha asociado con la emoción, el arousal y la atención. La AED depende de la activación de las glándulas sudoríparas y tiene un alto grado de sensibilidad (Wieland y mefferd, 1970), por lo que los cambios en la AED pueden entenderse como evidencia de variaciones en el estado cognitivo o emocional del sujeto (Hugdahl, 1995). Los niveles basales de AED pueden variar notablemente entre individuos e incluso en el mismo individuo en diferentes situaciones. Sin embargo, al analizar un mismo sujeto ante una misma situación, la respuesta disminuye con la habituación a ese estímulo para incrementarse ante la posterior aparición de un estímulo nuevo y decrecer de nuevo gradualmente a medida que se produce la habituación del mismo estímulo (Montagu, 1963). En situaciones de laboratorio, se produce un aumento de la conductancia durante la ejecución de la tarea (Siddle, Lipp y Dall, 1996), y una disminución al finalizar la misma (Köhler, Scherbaum y Ritz, 1995). Se han realizado diversos estudios de laboratorio sobre la respuesta electrodérmica ante estresores de tipo psicológico (Steptoe, Cropley y Joekes, 1999). En varios estudios realizados por Lazarus (1966), se encontró un aumento de los niveles tónicos de AED en individuos que veían escenas "estresantes" de largometrajes. Estos resultados se han encontrado también con varones hipertensos (Köhler y cols., 1995). La AED se ha

utilizado como indicador de estados de estrés (Clemens y Turpin, 2000) y como índice clínico en el estudio de diversos trastornos psicofisiológicos asociados con el estrés (Hugdahl, 1995).

En resumen, la FC y la AED reflejan hasta qué punto un estresor concreto puede producir un incremento en la activación autonómica. Ambas medidas pueden presentar un patrón de activación similar o diferente ante un mismo estímulo, por lo que podrían estar aportando información de diversos aspectos de un mismo proceso como es la respuesta al estrés (Moya y Salvador, 2001).

Capítulo 4

Cerebro y obesidad

1. Singularidades psicobiológicas del neurodesarrollo de la adolescencia

Durante la adolescencia se producen importantes cambios a nivel físico (crecimiento, cambios en la masa corporal, maduración sexual), psicológico (intensidad y labilidad afectiva, aspiraciones románticas e idealistas, sentido de invulnerabilidad, pensamiento abstracto) y social (distanciamiento de los adultos y niños, primacía de las relaciones entre compañeros, participación romántica) (Ernst, Pine y Hardin, 2006). Por lo tanto, el comportamiento en la adolescencia se ve afectado por multitud de factores. Distintos modelos teóricos han intentado explicar la regulación comportamental en la adolescencia. El modelo triádico de la neurobiología de la conducta motivada en la adolescencia de Ernst y cols. (2006), indica que la adolescencia se caracteriza por una descompensación madurativa entre los sistemas cerebrales encargados de procesar las recompensas (sistema fronto-estriado), los cuales están totalmente maduros en esta etapa, y los sistemas prefrontales encargados de la supervisión de la conducta, los cuales aún permanecen en desarrollo. A esta peculiaridad se añade un sistema de evitación de daños débil (amígdala), lo cual conlleva al adolescente a una mayor propensión a involucrarse en conductas de riesgo, como puede ser el consumo de sustancias de abuso. En resumen, según este modelo existe un aumento de la dominancia de las regiones motivacionales subcorticales en comparación con las regiones prefrontales. Aplicado a los problemas de exceso de peso, según este modelo, los adolescentes podrían sobreestimar las propiedades reforzantes y hedónicas de los alimentos apetecibles (altos en grasas y/o azúcares) restando importancia al equilibrio homeostático que regula el apetito. Esta situación conllevaría a la sobre ingesta ignorando las necesidades fisiológicas de hambre y saciedad y, a su vez, sin tener en cuenta las consecuencias negativas que este comportamiento podría tener sobre su salud.

Otros autores, como Chambers, y cols., 2003, se centran en las capacidades de autorregulación y control inhibitorio del adolescente, argumentando también la falta de maduración del PFC. La relativa maduración del sistema de recompensa conlleva una mayor vulnerabilidad a involucrarse en nuevas experiencias relacionadas con la recompensa. Estas actividades a su vez favorecen la maduración del PFC, pero suponen una vulnerabilidad hacia comportamientos donde las habilidades de autorregulación y control de impulsos son necesarias. Debido a esto, los adolescentes podrían ser más vulnerables a la ingesta de alimentos altos en grasas y/o azúcares debido los déficits nombrados anteriormente.

Por otro lado, Galvan, Hare, Voss, Glover y Casey (2007), además de señalar la descompensación entre los sistemas subcorticales y prefrontales, enfatizan el papel de la toma de riesgos en la adolescencia debido al aumento de la actividad del núcleo accumbens (NAcc) (Galvan y cols., 2007; Spear, 2000). En relación a la obesidad, podemos decir que los hábitos alimenticios no saludables podrían ser una conducta de riesgo hacia la que los adolescentes serían más proclives debido al déficit en el control de impulsos, su mayor sensibilidad a la recompensa y la mayor propensión hacia la toma de riesgos.

Por último, desde el modelo del marcador somático de Damasio (2006), se propone que en las personas que tienden hacia conductas de riesgo como el consumo de sustancias podría existir una ausencia, alteración o debilitamiento de los marcadores somáticos, lo que conduciría a tomar decisiones inadecuadas o desventajosas. Este déficit en los marcadores somáticos afectaría a la capacidad para decidir en función de las potenciales consecuencias futuras de la conducta, en lugar de en función de las consecuencias inmediatas. El modelo del marcador somático podría explicar la “miopía hacia el futuro” que presentan las personas con antecedentes de abuso de sustancias manifestada

en la alteración de la toma de decisiones. Este modelo propone también una alteración en el sistema fronto-estriado. Si aplicamos este modelo a la adolescencia, y tenemos en cuenta lo comentado anteriormente, podría explicar por qué los adolescentes con exceso de peso no son capaces de tener en cuenta las consecuencias perjudiciales que sus hábitos alimenticios tienen sobre su salud (debido a un déficit en sus marcadores somáticos), lo que les lleva a seguir teniendo una toma de decisiones alterada y vinculada al consumo de alimentos no saludables.

En resumen, estos modelos tienen varios aspectos en común ya que proponen que los adolescentes tienen mayor sensibilidad a la recompensa, mayor tendencia a comportamientos impulsivos/compulsivos y un pobre funcionamiento ejecutivo, y todo esto conlleva una mayor vulnerabilidad hacia conductas o comportamientos de riesgo, como puede ser una excesiva ingesta de alimentos.

2. Sistemas cerebrales asociados al comportamiento alimenticio

El hipotálamo ha sido considerado tradicionalmente como el centro cerebral regulador de la ingesta o el apetito (Kimet y cols., 2006). Sin embargo, a nivel cerebral, no solo el hipotálamo es responsable del balance energético (Rolls, 2008). Las hormonas implicadas en la modulación de la actividad del hipotálamo (p.e., leptina, ghrelina o insulina), también modulan la actividad neuronal en regiones cerebrales cortico-límbicas, las cuales están implicadas en la motivación, procesamiento de recompensas y aprendizaje de hábitos, procesos muy relacionados con el comportamiento alimenticio (Farooqi y cols., 2007).

Por otro lado, el sistema de recompensa cerebral es un componente central para desarrollar y monitorear comportamientos motivados. Por lo tanto, el conocimiento de su funcionamiento es vital para comprender mejor el problema de la obesidad. La

percepción de la recompensa de los alimentos comienza con la información generada por las células receptoras del gusto oral que posteriormente se transmite al núcleo del tracto solitario (NTS) por fibras sensitivas aferentes. Desde el NTS, la información del gusto se transmite a múltiples áreas del cerebro posterior (p.ej., el núcleo parabraquial), el mesencéfalo (zona tegmental ventral o VTA) y el prosencéfalo (p.ej., NAcc, el estriado, el tálamo y la corteza cerebral) (Kelley, Baldo, Pratt y Will, 2005), que colectivamente perciben y discriminan entre diferentes gustos y texturas, asignándole un determinado valor reforzante. El procesamiento más alto de la información del gusto se realiza en la ínsula (córtex gustativo primario), mientras que el OFC integraría la información del gusto con características olfativas, visuales y cognitivas (córtex gustativo secundario) (Rolls, 2005). La respuesta de esta última área a los estímulos del gusto disminuye a medida que los alimentos son ingeridos, lo que implica la capacidad de integrar información gustativa y estados de saciedad. De acuerdo con esta hipótesis, la disminución de la activación del córtex gustativo secundario disminuye el valor de recompensa de los alimentos y, por lo tanto, contribuye al cese de la alimentación mediante proyecciones al estriado y la amígdala (Kringelbach, O'Doherty, Rolls y Adrews, 2003).

La valoración de la recompensa también implica la liberación de dopamina (DA) en las neuronas del VTA. Éstas, a su vez, se proyectan al NAcc, estriado y otras áreas cerebrales. La DA que actúa en estas áreas del prosencéfalo aumenta potencialmente el impulso para obtener un estímulo gratificante (es decir, aumenta el "deseo" de un alimento o fármaco en particular) (Kelley y cols., 2005; Kelley y Berridge, 2002).

En resumen, existe evidencia de que el procesamiento cerebral de las recompensas depende de una red cerebral compuesta por diversas regiones, incluyendo el estriado, el PFC, el cíngulo anterior, la ínsula o las áreas dopaminérgicas del mesencéfalo (Haber y

Knutson, 2009). Como hemos comentado, existe cierta especialización dentro de este sistema, por ejemplo, el estriado ventral está más enfocado a la valoración subjetiva que se le otorga a reforzadores relevantes como la comida o el dinero (Passamonti y cols., 2009), mientras que la ínsula anterior parece estar más relacionada con la integración de información interoceptiva (Craig, 2009).

En nuestras sociedades occidentales actuales, en las que, como hemos mencionado, existe total disponibilidad de comida y están repletas de señales de alimentos altos en grasas y/o azúcares, el individuo tiene que ser capaz de controlar la cantidad de alimento que ingiere. Así, el comportamiento alimenticio ha dejado de ser una cuestión relacionada con la supervivencia tornándose en una actividad que adquiere un valor hedónico y reforzante. Los sistemas implicados en el procesamiento de las recompensas y la toma de decisiones juegan un papel muy importante, incluso a veces obviando los sistemas de regulación metabólica. Es decir, el individuo no solo regula su comportamiento alimenticio en función de sus estados de hambre o saciedad, sino también en función de otras propiedades reforzantes presentes en la comida, como apariencia, sabor, textura, olor, etc. (Zheng y Berthoud, 2007). Por lo tanto, ante la visualización de alimentos altamente apetecibles o de gran aporte energético, las áreas del circuito de la recompensa pueden promover una mayor liberación de DA debido a la gran saliencia que tiene el estímulo y conllevar así a una mayor predisposición a la sobreingesta (Stice, Figlewicz, Gosnell, Levine y Pratt, 2013).

Numerosos estudios también han relacionado la ingesta excesiva y la obesidad con la descompensación entre los sistemas cerebrales encargados de otorgar el valor reforzante a la comida y los sistemas encargados del control ejecutivo. Como hemos dicho, las personas con obesidad asociarían la comida y en concreto los alimentos hipercalóricos a un valor subjetivo mayor. A su vez se produciría una disminución de la eficacia de los

sistemas prefrontales ejecutivos, lo que daría lugar a la impulsividad e incapacidad para inhibir su comportamiento y finalmente conllevaría comportamientos relacionados con la alimentación excesiva (Volkow y cols., 2008; Rolls, 2011).

En la adolescencia, la descompensación entre estos dos sistemas está más acentuada como mencionamos con el modelo triádico de la neurobiología de la conducta motivada en la adolescencia de Ernst y cols., 2006. Además, diferentes estudios han expuesto que los adolescentes con exceso de peso presentan mayor impulsividad y sensibilidad a la recompensa (Van den Bert y cols., 2011).

3. La "adicción" a la comida

Recientemente, se ha postulado un modelo teórico de adicción a la comida ("*food addiction model*") basándose en las similitudes existentes entre las alteraciones cerebrales que presentan las personas con trastornos adictivos a sustancias y las personas que tienen obesidad (Volkow y cols., 2013). Las drogas de abuso utilizan los mismos mecanismos neurales que modulan la motivación para consumir alimentos, por lo tanto, existe una superposición entre los circuitos cerebrales implicados en la pérdida de control y la ingesta excesiva de alimentos que caracteriza la obesidad y el consumo compulsivo de drogas propio de la adicción. La alteración de los circuitos cerebrales de DA es central en estas dos patologías.

Las neuronas dopaminérgicas residen en los núcleos del cerebro medio (VTA, y sustancia negra) que se proyectan al estriado (NAcc y el estriado dorsal), regiones límbicas (amígdala e hipocampo) y regiones corticales (PFC, giro cingulado y córtex temporal) y modulan la motivación y el esfuerzo necesario para lograr los comportamientos de supervivencia. Para lograr sus funciones, las neuronas DA reciben proyecciones de regiones cerebrales involucradas con respuestas autonómicas (es decir,

hipotálamo, tronco cerebral), memoria (hipocampo), reactividad emocional (amígdala), excitación (tálamo) y control cognitivo (PFC y córtex cingulado) a través de una vasta matriz de neurotransmisores y péptidos. Por lo tanto, los neurotransmisores implicados en los comportamientos de búsqueda de drogas también están implicados en la ingesta de alimentos, y, por otro lado, los péptidos que regulan la ingesta de alimentos también influyen en los efectos reforzantes de las drogas. Sin embargo, y a diferencia de las drogas de abuso cuyas acciones están desencadenas por sus efectos farmacológicos directos en las vías DA de recompensa cerebral (NAcc y núcleo pálido ventral), la regulación de los comportamientos alimenticios está modulada por múltiples mecanismos periféricos y centrales que directa o indirectamente transmiten información a las vías dopaminérgicas, dónde el hipotálamo juega un papel primordial.

Ambos problemas pueden ser definidos como desordenes en los cuáles la saliencia de un tipo específico de recompensa (comida o droga) se valora exageradamente a expensas de otros tipos de reforzadores incrementando repentinamente la DA en los centros cerebrales de recompensa. En individuos vulnerables, estos incrementos de DA pueden invalidar a los mecanismos de control homeostático. Estudios de imagen cerebral han empezado a delinear algunos de los circuitos cerebrales superpuestos cuyas disfunciones pueden ser la base de los déficits observados. Los resultados sugieren que tanto los individuos obesos como los adictos a sustancias de abuso sufren alteraciones en las vías dopaminérgicas que regulan los sistemas neuronales asociados no solo con la sensibilidad de la recompensa y la motivación de los incentivos, sino también con el condicionamiento, el autocontrol, la reactividad del estrés y la conciencia interoceptiva (Volkow y cols., 2013) (ver figura 2).

El modelo de adicción a la comida ha sido ampliamente estudiado en los últimos años. Sin embargo, existen corrientes contrarias que han relacionado estos paralelismos entre

adicción y obesidad con patrones específicos de sobreingesta como el trastorno por atracón o “binge eating”, más que con el concepto de obesidad en sí (Ziauddeen y Fletcher, 2013). Esta condición se clasifica como un trastorno alimentario en el DSM-V y se caracteriza por episodios recurrentes ("atracones") de consumo incontrolado de gran cantidad de alimentos que se realiza de forma muy rápida, normalmente estando la persona sola e incluso en ausencia de hambre. Esta alimentación persiste a pesar de la incomodidad física y los atracones se asocian con marcada angustia y sentimientos de culpa y disgusto. Los atracones pueden desencadenarse por estados de ánimo negativos que no necesariamente mejoran por el atracón (Stein y cols., 2007). Una advertencia importante es que, aunque el trastorno por atracón o “binge eating disorder (BED)” se asocia con la obesidad, un número considerable de personas que muestran un comportamiento de atracones no presentan obesidad y la mayoría de las personas obesas no tienen este trastorno (Striegel-Moore y cols., 2001). Esta observación enfatiza la importancia de evitar el uso simple del IMC como un marcador general para el consumo compulsivo excesivo y comportamientos adictivos. También, recientemente ha aparecido un modelo alternativo postulando un cambio en la denominación, cambiando el concepto “food addiction” a “eating addiction”, el cual sugiere más bien una adicción comportamental al acto de comer, y no tanto al alimento en sí (Hebebrand y cols., 2014). Las personas que comen en exceso generalmente no restringen sus dietas a nutrientes específicos; en cambio, la disponibilidad de una gama más amplia de alimentos apetecibles (altos en grasas y/o azúcares) parece hacer que los sujetos propensos sean vulnerables a comer en exceso. Sin lugar a dudas, la industria alimentaria tiene que actuar de manera responsable, dado que el acceso fácil a alimentos altamente apetecibles y con alto contenido calórico promueve la ingesta excesiva y potencialmente el desarrollo de una "adicción a comer" (“eating addiction”) en personas

predispuestas. Además, los autores que apoyan este cambio de concepto postulan que el término "eating addiction" es más apropiado para evitar la connotación infundada de que la comida puede contener sustancias químicas que pueden conducir al desarrollo de un trastorno por consumo de sustancias, ya que el concepto de "adicción a comer" se asociaría más a una adicción comportamental (Hebebrand y cols., 2014).

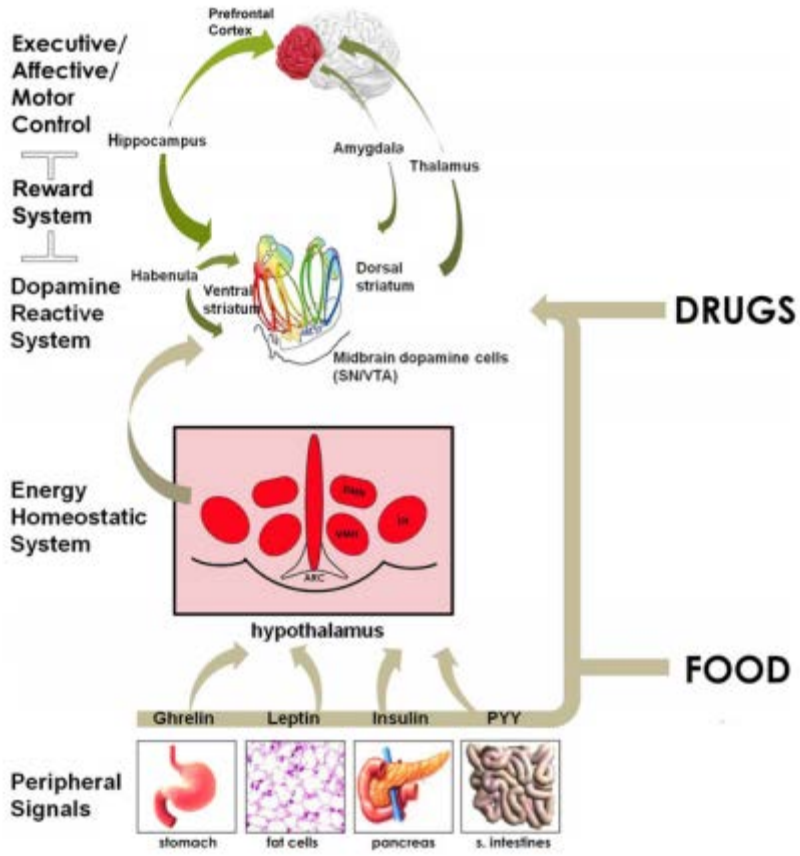


Figura 2. Mecanismos de acción de las drogas de abuso y la comida sobre las vías de recompensa cerebrales.

En contraste con las drogas de abuso cuyas acciones son desencadenadas por sus directos efectos farmacológicos en el sistema cerebral de recompensa mediado por la dopamina (área tegmental ventral, núcleo accumbens y pálido ventral), la regulación del comportamiento alimenticio y, por tanto, las respuestas a la comida están moduladas por múltiples mecanismos centrales y periféricos que directamente o indirectamente transmiten a las vías de recompensa cerebrales, incluidos aquellos envueltos en el placer, aversión, habituación y control cognitivo. PYY: peptide YY; s. intestines: small intestines; SN: substantia nigra (Adaptado de Volkow y cols., 2013b).

4. Estudios de activación cerebral relacionados con la motivación por la comida

En los últimos años ha aumentado exponencialmente el número de estudios que, utilizando fMRI, han analizado el funcionamiento cerebral de personas con obesidad, utilizando para ello distintos tipos de tareas. Los estudios de actividad cerebral se basan en mediciones de la señal BOLD (bloodoxygen- level-dependent) obtenida durante adquisiciones de fMRI (Ogawa y cols., 1993). De forma resumida, esta técnica se basa en que la actividad neuronal provoca cambios en la ratio oxihemoglobina /desoxihemoglobina, que son captados por un escáner de resonancia magnética, y transformados en imágenes. Los estudios de fMRI permiten obtener mapas de activación cerebral que reflejan las áreas implicadas en determinados procesos cerebrales. Para ello la persona evaluada simplemente debe realizar una determinada tarea dentro del escáner.

Un gran número de estudios han permitido estudiar la estructura y el funcionamiento cerebral de personas con exceso de peso. Como hemos comentado, determinados mecanismos neuronales tienen un papel crucial en los comportamientos alimenticios a través de la regulación de la motivación por la comida y el control del comportamiento (DelParigi, Pannacciulli y Tataranni, 2005). El análisis del procesamiento cerebral de estímulos alimenticios ha sido el paradigma más utilizado dentro de los estudios de neuroimagen con fMRI. Estos estudios en participantes sanos han mostrado que la comida es un potente reforzador cerebral y tanto su simple observación en imágenes, como su consumo, activan áreas del sistema de recompensa cerebral (O'Doherty, Deichmann, Critchley y Dolan, 2002; Kringelbach, y cols., 2003).

En cuanto a los resultados en obesidad, los estudios de fMRI indican que los individuos con obesidad muestran una mayor activación en la ínsula, el opérculo frontal, el OFC, la amígdala y el cuerpo estriado en respuesta a imágenes de alimentos apetecibles (Rothemund y cols., 2007; Stoeckel y cols., 2008) y a la recepción anticipada de estos (Stice, Spoor, Bohon, Veldhuizen y Small, 2008). Los datos sugieren que la ínsula y el opérculo frontal están involucrados en el deseo o "craving" a estos alimentos y a su recompensa anticipada, y además que el OFC, la amígdala y el cuerpo estriado codifican su valor de recompensa (Gottfried, O'Doherty y Dolan, 2003; Small, Veldhuizen, Felsted, Mak y McGlone, 2008).

En cuanto a los adolescentes, hay un menor número de estudios al respecto. Un estudio de Bruce y cols. (2010) encontró que el grupo de adolescentes con obesidad mostraba significativamente mayor activación que los adolescentes con un peso saludable ante las imágenes de comida en PFC (antes de comer) y en la OFC (después de comer). Además, el grupo con obesidad mostró menos reducción de la activación después de la comida en el PFC, y regiones límbicas y de procesamiento de la recompensa, incluyendo el NAcc. Asimismo, se ha observado el incremento de la activación en el córtex dorsolateral (dlPFC) en adolescentes con obesidad debido al aumento del control inhibitorio durante la visualización de alimentos (Davids y cols., 2010). Sin embargo, en un estudio de Batterink, Yokum y Stice (2010) donde se utilizaba una tarea específica go/no go de comida, los resultados mostraron que las adolescentes con sobrepeso mostraban mayor impulsividad en la tarea y menor activación de las regiones frontales inhibitorias. Esta variedad de resultados puede deberse a la diferencia en el paradigma utilizado.

En otro estudio con fMRI (Stice y cols., 2008), en el que se utilizaba un alimento apetitoso (batido de chocolate) y una solución insípida, las adolescentes con obesidad

mostraron una mayor activación bilateral que las adolescentes con peso normal en la corteza gustativa (ínsula anterior y media, opérculo frontal) y en las regiones somatosensoriales (opérculo parietal y opérculo rolandiano) en respuesta a la anticipación de la ingesta de batido de chocolate (frente a la solución insípida) y al consumo real de batido (frente a una solución insípida); estas regiones cerebrales codifican los aspectos sensoriales y hedónicos de los alimentos. Por otro lado, en un estudio de Yokum, Ng y Stice (2011) con chicas adolescentes, se observó que el IMC correlacionaba significativamente con la activación en regiones cerebrales relacionadas con la atención y la recompensa alimenticia, incluida la ínsula anterior, opérculo frontal, OFC, la corteza prefrontal ventrolateral (vlPFC) y el lóbulo parietal superior, durante la orientación inicial a señales de alimentos apetitosos. El incremento de activación en OFC durante la orientación inicial a alimentos apetitosos predijo futuros aumentos en el IMC. Los resultados indicaron que el sobrepeso estaba asociado a un mayor sesgo atencional a las señales de alimentos y que los adolescentes que mostraban mayor reactividad en los circuitos de recompensan durante la exposición a alimentos apetitosos tenían un mayor riesgo de aumento de peso.

En general, los resultados de los estudios de neuroimagen realizados hasta ahora señalan una respuesta incrementada en áreas del circuito de la recompensa, tanto en adultos como en adolescentes con exceso de peso, al procesar imágenes de comida, especialmente aquellas con un alto contenido en grasas y azúcares.

II. JUSTIFICACIÓN, OBJETIVOS E HIPÓTESIS

Capítulo 5

Justificación, objetivos e hipótesis de la tesis

1. Justificación y objetivo principal

Los cambios producidos en la sociedad actual en los últimos años han modificado la forma en la que percibimos e interpretamos el valor hedónico de los alimentos. Actualmente, nuestro ambiente, repleto de señales de alimentos altos en calorías y/o azúcares, hace necesario el fortalecimiento de los sistemas de control del comportamiento para poder resistir la tentación y evitar la sobreingesta. Como hemos dicho, no solo los mecanismos regulatorios homeostáticos son los responsables de nuestro comportamiento alimenticio, sino que otros muchos factores están influyendo en nuestra toma de decisiones a la hora de comer. Estas variables pueden ser la mayor palatabilidad de la comida, la extensa variedad de alimentos, alimentos baratos de fácil y rápido acceso, la continua presencia de señales alimentarias, la mayor densidad de energía en los alimentos, el mayor tamaño de las porciones, etc.

El aumento de la prevalencia del sobrepeso y la obesidad en edades cada vez más tempranas como es la niñez y la adolescencia, hace necesario investigar los mecanismos específicos que están actuando en esta población. El sobrepeso en la adolescencia está asociado con un mayor número de problemas y mayor severidad de estos en la edad adulta (Whitaker, Wright, Pepe, Seidel y Dietz, 1997). Aparte de las perjudiciales consecuencias del exceso de peso a nivel médico (p.ej., aumento de la diabetes tipo II en niños y adolescentes), los adolescentes con exceso de peso están expuesto a un mayor nivel de estrés social (p.ej., burlas, discriminación, bullying, etc.). Dado los efectos que produce el estrés crónico sobre las habilidades y recursos personales, es necesario indagar sobre las consecuencias del estrés social en adolescentes con exceso de peso. Además, las alteraciones neurocognitivas y emocionales que parecen estar relacionadas

con la obesidad podrían estar acentuadas en esta etapa debido a las peculiaridades en el neurodesarrollo que acontecen en la misma (Ernst y cols., 2006).

En este contexto es donde se encuadra la realización de esta tesis doctoral.

El **objetivo principal** de esta tesis es estudiar los mecanismos neuropsicológicos y cerebrales asociados al exceso de peso en adolescentes.

2. Objetivos específicos

De nuestro objetivo general se derivan tres objetivos específicos:

I. Primer objetivo: caracterizar y comparar la influencia del estrés social sobre el rendimiento neuropsicológico en adolescentes con exceso de peso y adolescentes con normopeso.

Este objetivo fue dividido en dos objetivos específicos:

1. Objetivos específico 1: caracterizar y comparar la influencia del estrés social sobre las funciones cognitivas de atención y toma de decisiones y sobre la respuesta de cortisol salival en adolescentes con exceso de peso y adolescentes con normopeso.
2. Objetivo específico 2: caracterizar y comparar la influencia del estrés social y el papel de la evaluación social negativa sobre tareas de función ejecutiva y medidas de reactividad psicofisiológica en adolescentes con exceso de peso y adolescentes con normopeso.

II. Segundo objetivo: evaluar y comparar la influencia de la visualización de estímulos alimenticios en una tarea de elección sobre el comportamiento en una tarea de toma de riesgos, y su relación con variables de impulsividad y niveles

de hambre subjetiva, en adolescentes con exceso de peso y adolescentes con normopeso.

III. Tercer objetivo: comparar los patrones de activación cerebral de un grupo de adolescentes con exceso de peso y un grupo de adolescentes con normopeso ante la visualización de una tarea de elección alimenticia, analizando la relación de esta activación con el *craving* provocado por los alimentos de la tarea.

Nuestro primer objetivo fue estudiar la influencia del estrés social sobre el rendimiento neuropsicológico en adolescentes con exceso de peso, ya que como hemos visto anteriormente, el estrés social es mucho más frecuente en esta población y además hay varias investigaciones que exponen la existencia de un menor rendimiento neuropsicológico en personas con obesidad. Por lo tanto, derivado de los resultados que abordan los perjudiciales efectos del estrés en la cognición, queríamos observar si la exposición al estrés social propiciaba una ejecución más pobre en adolescentes con exceso de peso en tareas que evaluaban distintas funciones cognitivas. Para ello realizamos dos estudios. En el primer estudio nos centramos en las funciones de atención y toma de decisiones y utilizamos la medida de cortisol salival como medida objetiva del estrés. Este estudio ha sido publicado en la revista Plos One (Verdejo-Garcia, A., Moreno-Padilla, M., Garcia-Rios, M. C., Lopez-Torrecillas, F., Delgado-Rico, E., Schmidt-Rio-Valle, J., & Fernandez-Serrano, M. J., 2015) y se encuentra íntegramente en el Capítulo 6 de esta tesis. En el segundo estudio evaluamos el resto de funciones ejecutivas (memoria de trabajo, inhibición y flexibilidad) y utilizamos la reactividad psicofisiológica (tasa cardíaca y respuesta electrodermal) como medida objetiva del estrés. Además, también analizamos el efecto específico de la evaluación social negativa, ya que los adolescentes con exceso de peso están expuestos con mayor frecuencia a las evaluaciones sociales despectivas (normalmente por parte de sus

iguales). Este estudio ha sido publicado en la revista Annals of Behavioral Medicine (Moreno-Padilla, M., Fernández-Serrano, M. J., Verdejo-García, A., & Reyes del Paso, G. A, 2018) y se encuentra íntegramente en el Capítulo 7 de esta tesis.

Respecto al objetivo 2, nuestro planteamiento estuvo basado en los resultados de distintos estudios que han mostrado que la visualización de señales relacionadas con el consumo de drogas produce un incremento en los niveles de impulsividad e induce a una mayor toma de riesgos en individuos adictos a sustancias, incrementando como consecuencia el riesgo de consumo. En este contexto realizamos un tercer estudio en el que, dadas las similitudes encontradas entre los sistemas que regulan la adicción a sustancias y la obesidad, investigamos la influencia de la visualización de imágenes de comida sobre la toma de decisiones en adolescentes con exceso de peso. Este estudio está bajo revisión en la revista Plos One y se encuentra íntegramente en el Capítulo 8 de esta tesis.

En cuanto al objetivo 3, queríamos estudiar las diferencias en activación cerebral entre los dos grupos ante una tarea de elección alimenticia y comprobar, si como aparece en los individuos adictos a sustancias, esta activación está relacionada con el *craving* por alimentos con alta saliencia (algos en grasas y/o azúcares). Para abordar este último objetivo realizamos nuestro cuarto estudio que está bajo revisión en la revista Appetite y se encuentra íntegramente en el Capítulo 9 de esta tesis.

3. Hipótesis

Las principales hipótesis que se derivan de estos objetivos son:

I. Los adolescentes con exceso de peso serán más sensibles a la influencia del estrés social y presentarán peor rendimiento en las tareas de atención y toma de

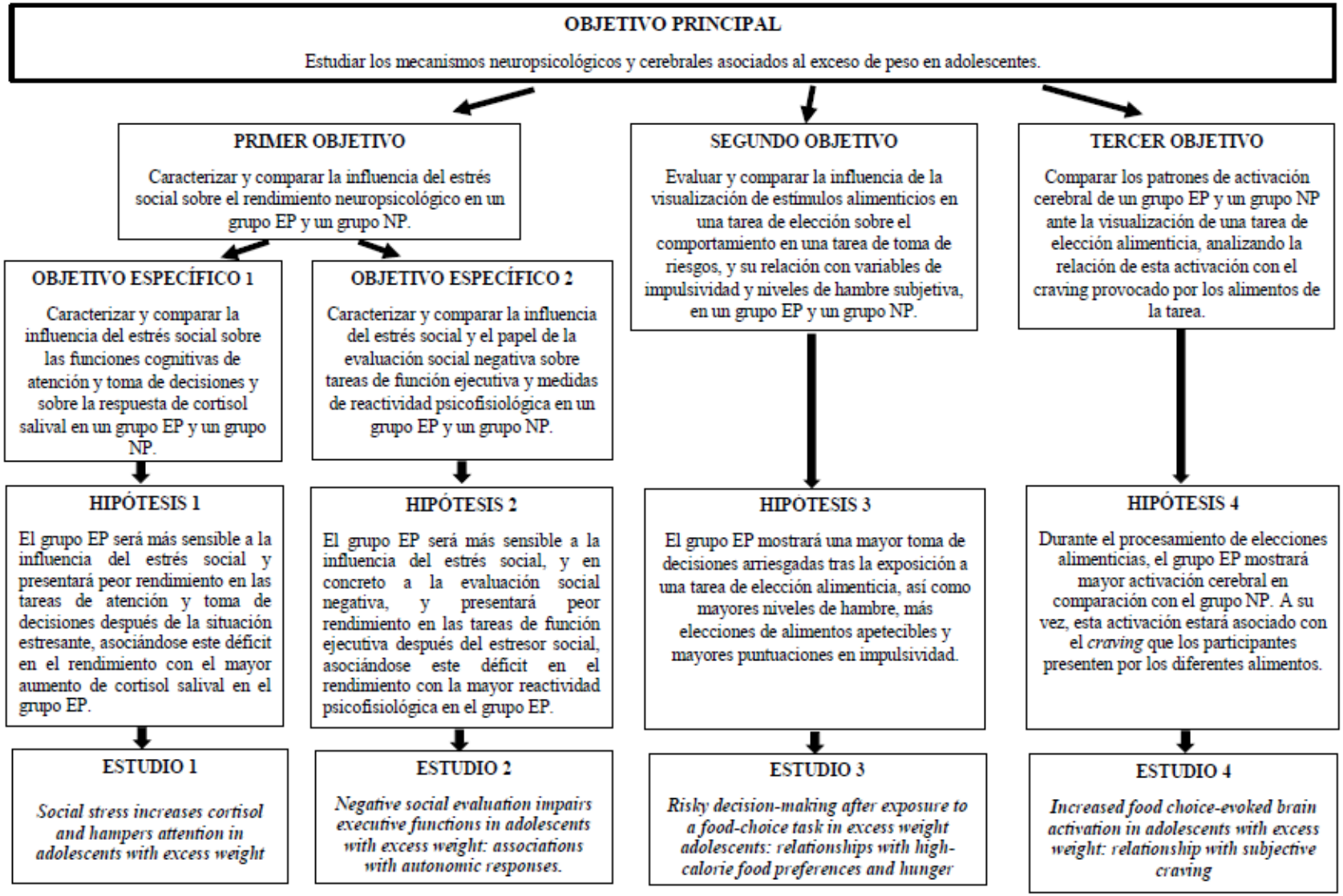
decisiones después de la situación estresante, asociándose este déficit en el rendimiento con el mayor aumento de cortisol salival en adolescentes con exceso de peso.

II. Los adolescentes con exceso de peso serán más sensibles a la influencia del estrés social, y en concreto a la evaluación social negativa por parte de la audiencia, y presentarán peor rendimiento en las tareas de función ejecutiva después del estresor social, asociándose este déficit en el rendimiento con la mayor reactividad psicofisiológica en adolescentes con exceso de peso.

III. Los adolescentes con exceso de peso mostrarán una mayor toma de decisiones arriesgadas tras la exposición a una tarea de elección alimenticia, así como mayores niveles de hambre, más elecciones de alimentos apetecibles y mayores puntuaciones en impulsividad.

IV. Durante el procesamiento de elecciones alimenticias, los adolescentes con exceso de peso evidenciarán mayor activación cerebral en comparación con los adolescentes con normopeso. A su vez, esta activación estará asociado con el *craving* que los participantes presenten por los diferentes alimentos.

(Ver figura 3).



EP: exceso de peso; NP: normopeso

III. MEMORIA DE TRABAJOS

<u>Capítulo 6.</u> Social stress increases cortisol and hampers attention in adolescents with excess weight

Verdejo-Garcia, A., Moreno-Padilla, M., Garcia-Rios, M. C., Lopez-Torrecillas, F., Delgado-Rico, E., Schmidt-Rio-Valle, J., & Fernandez-Serrano, M. J. (2015). Social stress increases cortisol and hampers attention in adolescents with excess weight. *PloS one*, *10*(4), e0123565. doi: 10.1371/journal.pone.0123565

1. Introduction

Adolescents with excess weight suffer substantial social stress including frequent peer bullying and social marginalization and exclusion [1,2]. Crucially, the degree of exposure to these social stressors is the most important predictor of poor psychological adjustment and poor academic achievement in adolescents with obesity [3]. Moreover, neuroendocrine studies have shown that non-fasting levels of the "hunger hormone" ghrelin increase in response to social stressors (i.e., the Trier Social Stress Task, involving a public speak) [4] and that the awakening response of the "stress hormone" cortisol positively associates with subsequent lipid intake [5]. Therefore, social stress is a potent determinant of poor cognition and poor food choices in adolescents with excess weight. This phenomenon could be explained by the harmful impact of social stress on cognitive skills such as attention, cognitive control and decision-making, which contribute to obesity-related behaviours in adolescents [6]. The harmful impact of persistent social stressors on cognition in adolescents with obesity is likely to be enduring as stress induces neuroadaptations in prefrontal and limbic regions particularly during adolescence [7,8]. Therefore, examining whether social stress hampers cognition in adolescents with excess weight is essential for prevention of cognitive decline and hence progression of obesity. However, to date no studies have experimentally assessed this notion. In this study we examined if a social stressorthe Trier public speaking stress task- specifically increases cortisol levels and hampers cognitive performance in adolescents with excess weight compared to adolescents with normal weight. We specifically assessed the impact of social stress on outcome measures of attention, cognitive inhibition and decision-making. We selected these outcomes because they reflect the function of frontal-limbic systems [9,10] and are longitudinally associate with weight gain in pediatric populations [11,12]. We hypothesized that adolescents

with excess weight would show greater cortisol response to the social stressor, and greater detrimental impact of social stress on attention and decision making performance.

2. Methods

Participants

Eighty-four adolescents aged between 12 and 18 years old participated in the study. They were classified in two groups (Normal weight [n = 42] and Excess weight [n = 42]) based on their age adjusted Body Mass Index (BMI) percentile [13]. Sample size was estimated through power analysis. The existing evidence about the impact of the Trier Social Stress Task (TSST) on selected outcome variables was correlational (i.e., the association between TSST-induced cortisol changes and decision-making performance is between 0.3 and 0.4) [14,15]. Therefore, we estimated that in order to achieve adequate power (80%) to detect a $\rho H1 = 0.3$ association between the independent variable (stress) and the cognitive outcomes (attention and decision-making) 84 participants would be required. This sample size was deemed acceptable for the mixed repeated-measures design. The classification of the two groups was conducted in alignment with the guidelines of the International Obesity Task Force and the Centers for Disease Control and Prevention: Normal weight participants had age adjusted BMI percentiles in the range between the 5th and the 84th percentile, and Excess weight participants had age adjusted BMI percentiles 85 (Table 1). Three participants from the Excess weight group provided invalid cortisol samples, and therefore the final study sample comprised 42 Normal weight and 39 Excess weight participants. Participants' socio-demographic characteristics, BMIs, percentage fat and blood count obtained biochemical parameters are as well displayed in Table 1. Participants also completed The Dutch Eating Behavior Questionnaire [16] which was

used to characterise psychological traits relevant to maladaptive eating behaviours (i.e., external eating, emotional eating and restraint) (Table 1). Participants were recruited from the paediatrics and endocrinology services of the Hospital "Virgen de las Nieves" in Granada (Spain), and from schools located in the same geographical area. The inclusion criteria for participants were defined as follows: (i) age range between 12 and 18 years old; (ii) BMI percentiles falling within the intervals categorized as overweight or obesity (85—Excess weight group), or normal weight (5–85—Normal weight group); and (iii) absence of history or current evidence of neurological or psychiatric disorders, assessed by participants and parent's interviews and the Eating Disorder Inventory [17]. All participants had normal or corrected-to-normal vision.

Table 1. Descriptive scores for the demographic, biometric and blood count characteristics of adolescents with excess and normal weight.

	Excess weight		Normal weight			
Variables	Mean	SD	Mean	SD	t[a]/chi square[b]	p
Age	15.59	1.91	15.62	1.83	-.07[a]	.944
Gender (% Men/Women)	52.4/47.6		43.2/56.8		.72[b]	.262
BMI	29.87	3.57	20.87	2.06	13.73[a]	.000
Fat (%)	31.97	9.15	17.99	6.94	7.69[a]	.000
DEBQ						
Emotional	23.68	9.33	24.03	9.02	-0.17[a]	.858
External	28.64	7.11	31.28	7.68	-1.71[a]	.091
Restraint	25.55	7.22	19.30	7.81	3.98[a]	.000
Glucose	92.57	6.03	92.14	6.64	.276[a]	.783
Cholesterol	158.07	27.35	148.47	20.89	1,64[a]	.104
Triglycerides	70.64	28.76	63.13	27.32	1.09[a]	.279
HDL	56.80	12.49	58.73	12.82	-.61[a]	.541
LDL	90.85	21.08	80.51	14.96	2.38[a]	.020
Insulin	47.28	57.78	53.34	114.18	-.25[a]	.802
Uric Acid	5.08	0.87	4.39	0.97	2.98[a]	.004
Thyroxine	1.33	0.43	1.44	0.68	-0.79[a]	.451

[a]value of *Student's t;*
[b]value of *Chi-square* χ^2

Experimental procedures

Fig 1 displays a schematic representation of the experiment. In order to induce social stress in the laboratory we utilised a previously validated Virtual Reality version of the Trier Social Stress Task (TSST) [18]. Participants had to perform a stressing task which consisted of delivering a speech about personal characteristics including both positive and negative aspects of themselves in front of a simulated audience. Participants were

told that this audience would at- tend the speech and subsequently evaluate its quality. However, the virtual audience was programmed to look progressively bored and disappointed with the speech. The speech was followed by a mental calculation test (serially subtracting 17, starting from 2013). Cortisol levels were measured via saliva samples collected before onset of the TSST (T1), after completion of the TSST and the calculation test (10 minutes after TSST onset—T2) and after performance on each of the attention and decision making cognitive probes (20 and 30 minutes after TSST onset-T3 and T4- respectively). Cognitive measures were conducted in a fixed order before TSST onset (pre-TSST, overlapping with T1) and after completion of the TSST and the calculation test (post-TSST, overlapping with T2). To minimize practice effects, we utilised parallel versions of all tasks in the post-TSST administration. The original validation study showed that this virtual reality TSST is able to induce modest but sizeable increases in cortisol and subjective stress responses [18]. Moreover the virtual audience tamed the ethical concerns associated with the negative impact of the social stressor on adolescents' participants. The Ethics Committee for Human Research of the Universidad de Granada approved the study. Both participants and parents signed informed consent.

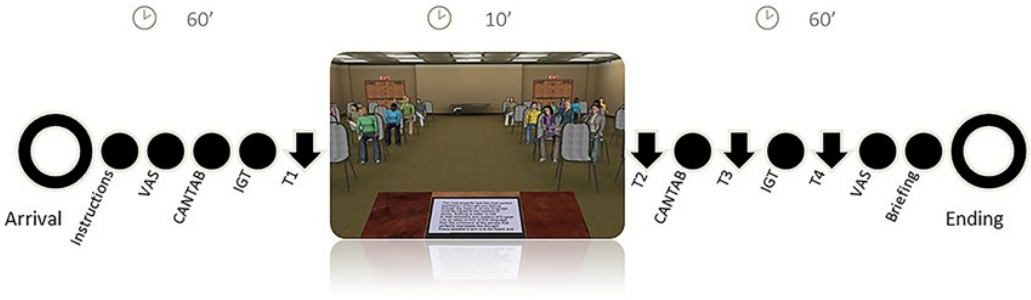


Fig 1. Schematic representation of the experiment.

Cortisol measurement. Participants were told not to smoke, eat or drink coffee for at least 30 minutes before the experiment. All the experimental sessions were conducted at

the same time of the day (4–5 pm) based on pilot data obtained in this cohort prior to study onset indicating that diurnal cortisol levels were stable during these hours. Saliva was collected via a commercially available device: Salivette Cortisol (Sarstedt, Numbrecht, Germany). This device is composed of a cotton tube (similar to dental cotton), and two plastic tubes that fit one inside the other. Subjects were told to place cotton salivettes inside their mouth and gently chew and/ or suck on them for 1–3 min until they became soaked in saliva. The cotton tube was inserted inside the plastic tube, which was then capped. Saliva samples were stored at -20°C until required for assay. Samples were analyzed at the University Hospital, using the electrochemiluminescence immunoassay "ECLIA" method. This method is designed for use in Roche Elecsys 1010/2010 automated analyzers and in the Elecsys MODULAR NALYTICS E170 module. We computed two different metrics from each cortisol sample (microgram/deciliter and nanomol/liter). The correlation between both metrics at the different time points ranged from 0.8 and 0.9.

Cognitive measures. We utilized three computerized tests: two subtests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) [19], Motor Screening (MOT) and Rapid Visual Information Processing (RVP), and the Iowa Gambling Task (IGT) [20]. Al- ternate versions of each test were used in pre-stress and post-stress administrations.

MOT. The main objective of this test is to provide a baseline measure of the subjects' basic motor skills in terms of reaction times and accuracy. After a demonstration of the correct way to point on the computer screen using the forefinger of the dominant hand, the subjects must point to a series of stimuli (crosses) popping up in turn. The outcome measure of this test was response latency.

RVP. This is a test of visual sustained attention with an impulse control component. A white box is displayed in the centre of the computer screen, inside which digits, from 2 to 9, are displayed in a pseudo-random order, at the rate of 100 digits per minute. The subject must detect consecutive odd or even sequences of digits (for example, 2-4-6) and respond by pressing the touch pad. The outcome measures of this test were response latency and response discriminability (B') scores, which are sensitive to attention and impulse control domains respectively. The B' score is the signal detection measure of the strength of trace required to elicit a response (range -1.00 to +1.00). Thus, it is the tendency to respond regardless of whether the target sequence is present and uses the p(hit) and p(fa) results. A score close to +1.00 indicates that the subject gave few false alarms.

IGT. This is a computer task measuring reward/punishment based decision-making. It involves four decks of cards (A, B, C and D). Each time a participant selects a card, a specified amount of play money is awarded. However, interspersed among these rewards, there are probabilistic punishments (monetary losses). Two of the decks of cards (A and B) produce high immediate gains; however, in the long run, they will take more money than they give, and are thus considered disadvantageous. The other two decks (C and D) are considered advantageous, as they result in small, immediate gains, but will yield more money than they take in the long run. The performance measure was the net score calculated by subtracting the number of dis- advantageous choices (decks A and B) from the number of advantageous choices (decks C and D). An equivalent parallel version of the ABCD task in which decks are labelled K, L, M and N was utilised in the post-TSST administration. These versions have shown adequate test-retest reliability and ecological validity in relation to decision-making [21].

Visual Analogue Scales (VAS). We used two Visual Analogue Scales (VAS) designed to rate arousal and stress. For arousal scale the individual must indicate the extent to which they perceived as active and alert (from nothing active to very active). For stress scale they must indicate how much stress they feel (from no stress to very much stress). We used the mean scores of each dimension.

Statistical analyses

The main hypotheses were examined utilizing mixed repeated measures analyses of variance including Time as the repeated-measures factor, Group as the between-groups factor, and cortisol levels (as measured in μg/dl) and RVP's mean response latency and B' scores and IGT's net scores as dependent measures. Cortisol and RVP performance measures were log-trans- formed (base 10) to meet the normal distribution, but for the sake of clarity the Figures report non-transformed measures. IGT scores fitted to the normal distribution as assessed by Kolgomorov-Smirnov tests. We also performed correlation analyses between change scores of cortisol levels (T2—T1) and change scores of cognitive performance (T2—T1) and between both change scores and biological and psychological measures. These change measures were non- normally distributed and therefore we applied Spearman's rank correlation analyses. Two participants from the Excess weight group (n = 37) and one participant from the Normal weight group had missing cortisol data at T1 and T2 (n = 41). With regard to cognitive tests, there was no missing data in the Excess weight group (n = 39), whereas in the Normal weight group three participants had invalid data for RVP response latency and IGT (n = 39) at T1 or T2, and three participants had invalid data for RVP B' (n = 38) at T1 or T2.

3. Results

Cortisol response

We found a significant Time x Group interaction on cortisol levels, F (3,74) = 4.36, p = 0.008. Cortisol mildly increased in Excess weight participants after the TSST. Independent-sample t- tests showed that Excess weight and Normal weight participants did not significantly differ on cortisol levels before TSST (T1). However, Excess weight adolescents showed significantly in- creased cortisol levels after TSST (T2), t = 1.94, p = 0.05, Cohen's d = 0.5 (Fig 2). Moreover, cortisol increase between T2 and T1 correlated with amount of fat, Spearman's Rho = 0.30, p = 0.01. Between-group differences were also statistically significant at T3, t = 2.44, p = 0.02, and T4, t = 2.63, p = 0.01. However, this effect seems to be driven by decreased cortisol levels in the Normal weight group (Fig 2).

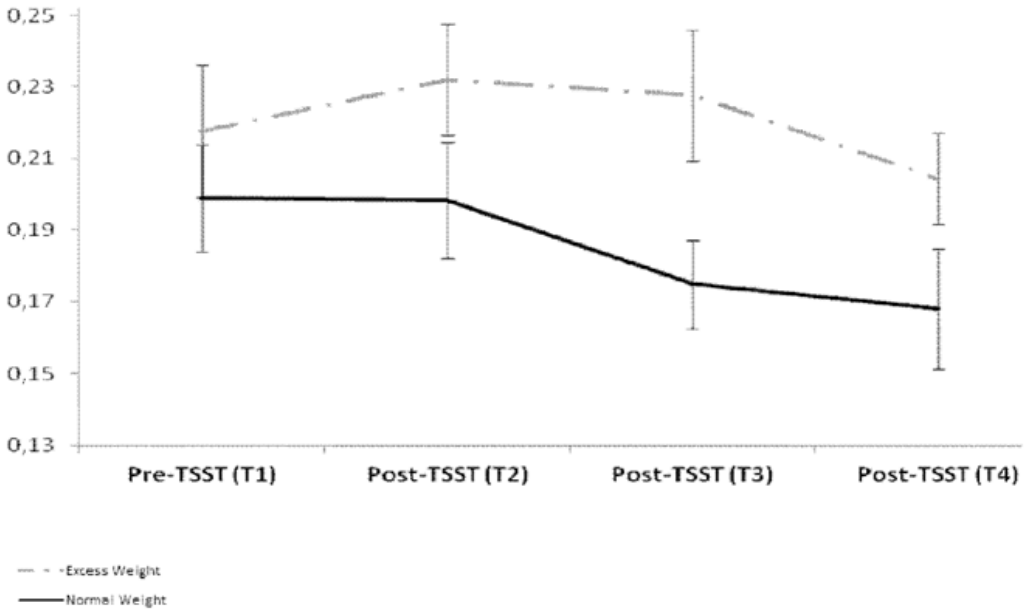


Fig 2. Cortisol levels (μg/dl units) in adolescents with excess weight and adolescents with normal weight before and after exposure to the Trier Social Stress Task (TSST). T1 represents cortisol levels before TSST; T2 represents cortisol levels immediately after TSST termination; T3 and T4 represents cortisol levels 10 and 20 minutes after TSST termination.

Cognitive performance

MOT. Pre-TSST scores showed that both groups had similar baseline response latencies. Further, both groups showed mild reductions of response latencies between the pre-TSST measure and the post-TSST measure (Fig 3).

RVP—Response latency. We found a significant Time x Group interaction, $F(1,76) = 6.35$, $p = 0.01$ (Fig 3). Independent-sample t-tests showed that Excess weight and Normal weight participants did not significantly differ in the pre-TSST measure. However, they showed marginally significant differences in the post-TSST measure, $t(78) = 1.75$, $p = 0.08$, Cohen's $d = 0.4$, with Excess weight participants performing significantly poorer than Normal weight controls. There was no significant correlation between T2—T1 cortisol levels and T2—T1 RVP Response Latency.

RVP—Response discriminability. We did not find a significant Time x Group interaction, $F(1,75) = 0.99$, $p = 0.32$. There were no main effects of Time or Group, although visual inspection shows Excess weight participants performed better than Normal weight participants in both pre- and post-TSST measures (Fig 3).

Decision-making—IGT. We did not find a significant Time x Group interaction, $F(1,77) = 0.005$, $p = 0.94$. There was a significant main effect of Time, $F(1,77) = 6.01$, $p = 0.02$, indicating that both groups exhibited significantly poorer performance after the TSST (Fig 3). There was no significant correlation between T2—T1 cortisol levels and T2—T1 IGT performance.

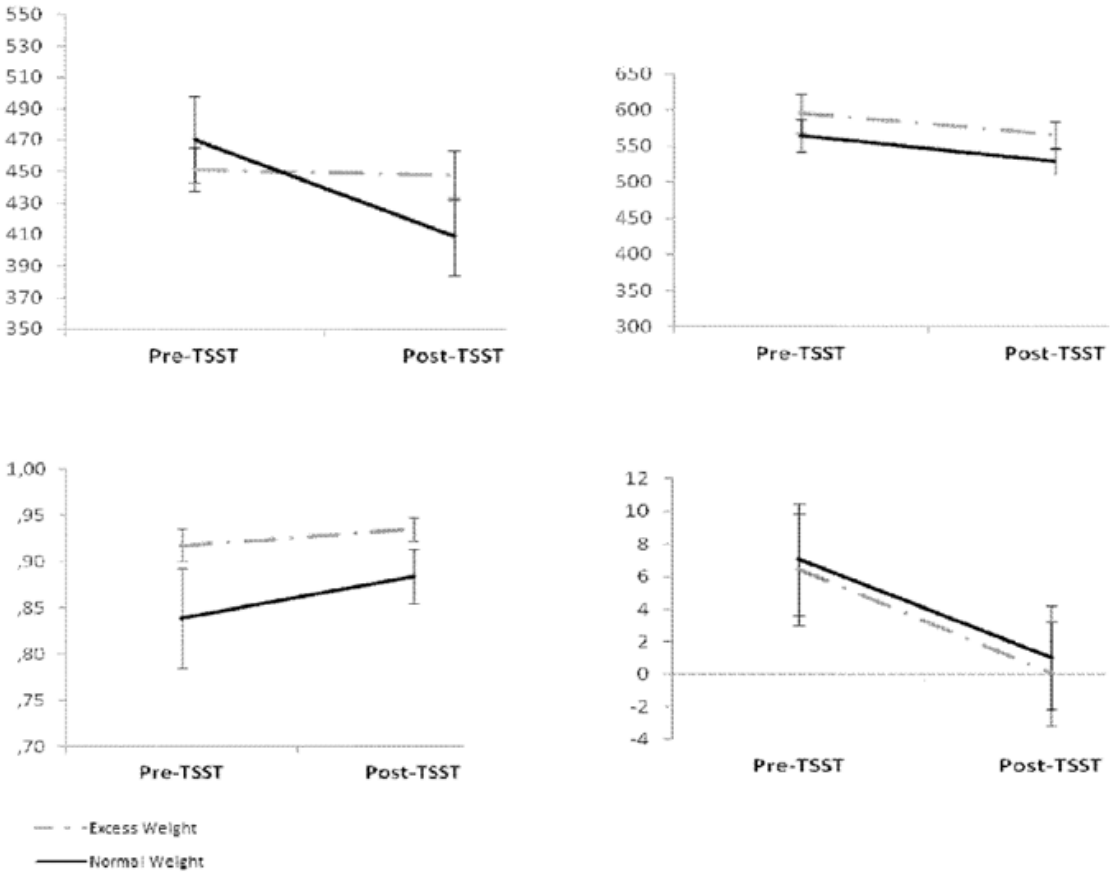


Fig 3. Cognitive performance in adolescents with excess weight and adolescents with normal weight before and after exposure to the Trier Social Stress Task (TSST). Top panel Y axes represent time in milliseconds. The Y axis in the bottom-left panel represents signal detection derived Beta scores, ranging from 0 to 1. The Y axis in the bottom-right panel represents Iowa Gambling Task net scores, ranging from -60 to +60.

Correlations between biological and psychological measures and cognitive performance in T2—T1. We found a positive correlation between levels of uric acid and change in RVSP response latency performance between T2 and T1, Spearman's Rho = 0.46, p = 0.0001, and a negative correlation between thyroxine levels and change in Iowa Gambling Task performance between T2 and T1, Spearman's Rho = -0.27, p = 0.03. We also found a negative correlation between scores of external eating and RVSP response latency performance between T2 and T1, Spearman's Rho = -0.27, p = 0.02.

Visual Analogue Scales (VAS). We did not find a significant Time x Group interaction on VAS of arousal or stress but results were in the expected direction, with both groups showing more subjective arousal and stress after the TSST.

Post-hoc analyses in the subsample of participants showing enhanced cortisol response. The primary analyses indicated that in the normal weight group cortisol levels did not change after stress, and therefore there is a concern that cognitive changes were due to spurious factors. To address this issue, we run additional analyses in the subsample of participants who showed sizeable increments in cortisol levels after stress, including 24 participants of the Excess weight group (57% of the original sample) and 20 participants of the Normal weight group (48% of the original sample). The results of these analyses were coherent with the main findings. We found a significant Time x Group interaction on RVP's latency scores, $F(1,41) = 6.17$, $p = 0.02$, whereby a drop in performance was only observed in the Excess weight group. Moreover, there was a significant correlation between T2—T1 cortisol levels and T2—T1 RVP Response Latency (Spearman's Rho = 0.25, punilateral = 0.05) (Fig 4).

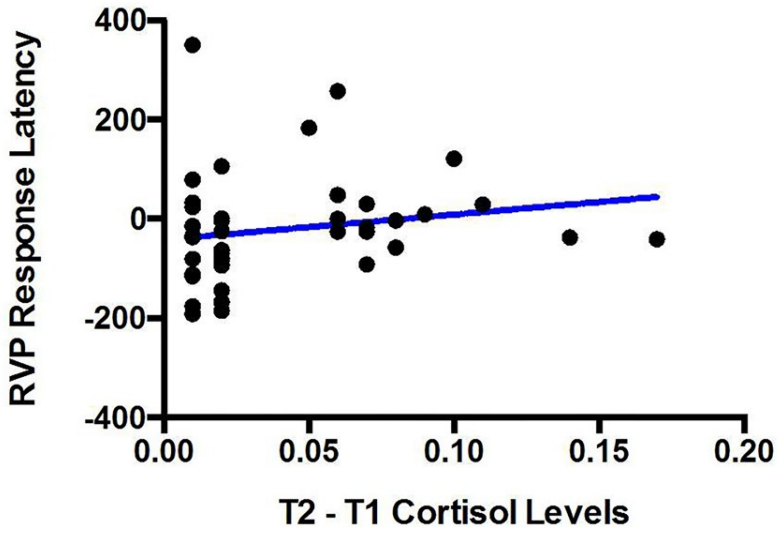


Fig 4. Correlation between between T2—T1 cortisol levels (X Axis) and T2—T1 RVP Response Latency (Y Axis) within the subsample of participants showing TSST-induced increases in cortisol levels.

4. Discussion

We show that social stress specifically increases cortisol levels and hinders attentional response latency in adolescents with excess weight. Conversely, social stress failed to show significant effects on attention response discriminability. Moreover, both excess weight and normal weight adolescents displayed poorer decision-making performance after the social stressor. These findings indicate that adolescents who are overweight and obese have enhanced stress reactivity in response to social stressors, which selectively impacts on attentional skills. Since adolescents with excess weight are markedly exposed to social stressors during everyday lives, our findings suggest that stress immunization strategies should be put in place to prevent the harmful impact of social stress on cognition and therefore on progression of obesity.

In agreement with our primary hypothesis, social stress induced greater cortisol response in overweight and obese adolescents. The effect was mild but the specific impact on participants with excess weight agrees with the notion that repetitive social stress may induce sensitization of the hypothalamic-pituitary-adrenal (HPA) axis [22] and purportedly of the HPA axis associations with fronto-limbic systems [23–25]. The discrepancy between our finding of cortisol in- crease and a previous negative finding in obese adults [26] suggests that adolescence compared to adulthood is a more sensitive time period for abnormal sensitization of stress systems, likely due to ongoing neural maturation of these systems [7,27]. Further, both preclinical and clinical evidence shows that social stressors such as social evaluation and social exclusion are particularly challenging for adolescents [8,28,29]. The potential mechanisms for the specific impact of social stress on stress reactivity in adolescents with excess weight include the additive or synergistic interactions between social stress and inflammation [30,31]

and/or between social stress and obesity-related neuroadaptations in anterior cingulate and limbic regions that are essential for stress regulation [32,33]. Our finding is particularly relevant in view of the significant association between cortisol reactivity and obesity-related behaviours [34,35], and of the emerging evidence suggesting that high levels of stress can longitudinally predict the progression of obesity [36].

We also showed a significant impact of social stress on attentional performance in adolescents with excess weight. The effect was again mild and pointed to stress-related hindering of the capacity to get benefit from a repeated administration of the task. Previous findings indicate that repeated administration of CANTAB attentional tests is associated with significant improvements in performance (of at least 0.3 in Cohen's d effect size) [37], and this is what we observed in the control group. However, excess weight adolescents were unable to get benefitted from this repeated administration. The effect was specific for attention-related latency adjustments, but not for psychomotor-related reaction times. Therefore, it suggests a detrimental impact of stress on attention regulation.6 This notion is consistent with the neural networks interactions between the HPA axis and medial prefrontal cortex and anterior cingulate cortex regions involved in attention regulation [38–40]. In support, neuroimaging studies have shown that the impact of stress on executive attention is mediated by structural (gray matter) neuroadaptations in prefrontal cortex and anterior cingulate cortex regions [41]. This stress-related attentional hurdle has a high translational value, as individual differences in response latencies to attentional probes are longitudinally associated with increases in BMI [12], implying that ad- equate control of social stress and/or cognitive boosting of attentional resources may contribute to prevent chronic obesity. This notion is consistent with our finding of significant correlations between less improvement of attentional performance (between T1 and T2) and higher maladaptive eating patterns

such as external eating, which reflects attentional bias to- wards food related cues. Further, both social stress and attentional skills are significantly associated with advantageous social functioning and academic performance [3], and therefore our finding highlights the potential benefit of controlling social stress to improve social and career outcomes in the long-term.

Furthermore, we found poorer decision-making after the social stressor in both adolescents with excess weight and adolescents with normal weight. Since cortisol levels dropped between T3 and T4 (the time window of decision-making task performance) it is unlikely that this finding can be attributed to the effects of acute stress. However, it might be attributed to broader effects of the social stressor, such as the social evaluation context. The latter notion agrees with previous experimental evidence showing that adolescents make riskier choices than young adults or adults when they are under social evaluation [42]. The lack of specificity of our result implies that the impact of social evaluation on decision-making is mediated by neural mechanisms that are similarly sensitized in adolescents regardless of BMI/weight status, or that different neural mechanisms mediate a similar impact of social evaluation on decision-making in excess weight and normal weight adolescents. In favour of the first notion, neuroimaging studies have shown that the impact of social evaluation on decision-making is mediated by increased activation of ventral striatal and orbitofrontal regions [43], which are generally sensitized during adolescence. In favour of the second notion, we have observed that excess weight and normal weight adolescents recruit different brain circuitries during the pondering of social decisions [44]. Future studies are warranted to address this question. In any case, our finding might have general implications for prevention of obesity during adolescence as we know that adolescents who are overweight or obese have higher exposure to social evaluations [3] and that

subsequent risky choices are longitudinally associated with weight gain and obesity [11].

We conclude that social stress response is sensitized in adolescents with excess weight, hindering their attentional function. The study has important strengths including the experimental design, the power-informed sample size, the detailed phenotypic characterization and the group matching of excess weight and normal weight adolescents, and the objective measurement of stress reactivity with cortisol biomarkers. However, the results should be as well appraised in light of relevant limitations. It is particularly important to stress that unlike the original TSST [45], the virtual reality TSST was not able to induce significant increases of cortisol levels in the control group. We selected this stressor because it was capable of inducing mild but sizeable stress in the laboratory at the same time that it reduced the ethical implications of stressing "at risk" obese adolescents [18]. In agreement with this assumption, our results indicate that the stress manipulation was actually more effective in obese adolescents (57% of participants showed increased cortisol levels) than in controls (only 48% of participants showed increased cortisol levels). There are however several factors that may explain the variability in stress induction, such as degree of belief in the cover story or degree of immersion in the virtual reality environment, that were not systematically controlled in this study. Therefore, further studies are warranted to reassess the validity of this virtual reality version, and to replicate our findings using TSST versions that are able to unequivocally reproduce the original TSST stress induction. Moreover, in absence of a "no-stress" control condition, we cannot ascertain a causal link between stress and cognitive performance. However, we base our interpretation on previous evidence showing that improvement (rather than stability or decrease) in performance is typically expected in "no-stress" repeated administration designs [37]. A related limitation is the

negative finding in relation to cognitive impulsivity. Since mild arousal improves inhibitory control in adolescents, it is plausible that the mild nature of the stressor fostered cognitive impulsivity increases rather than (expected) decreases after TSST. Future studies are warranted to address these limitations, to expand on the biological, psychological and socio-economic mediators of the impact of social stress on cognition, and to longitudinally assess the relevance of this experimental effect on public health indicators of the progression of obesity.

5. References

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Capítulo 7. Negative social evaluation impairs executive functions in adolescents with excess weight: associations with autonomic responses.

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1. Introduction

Overweight and obesity in adolescence have sharply increased over recent decades, reaching epidemic levels (1). The socioeconomic changes that have occurred in recent decades in Western societies, associated with the unlimited access to food, have modified the way we perceive food and regulate intake. These processes are increasingly influenced by a variety of factors besides homeostatic regulation, like sensory cues (e.g., taste, smell, texture and appearance), availability, motivational and affective states, pleasure seeking, etc. All of these factors influence what and how much people eat even when they are not hungry (2). In the last few years, obesity is being increasingly considered as a brain-related dysfunction similar to that occurring in addictions (3), where the motivational value of highly palatable food is significantly increased, while the top-down or executive control mechanisms that would normally regulate reward-driven responses are diminished (4, 5). Executive control mechanisms are relevant to the regulation of eating behavior (6), since they allow for adjustment of behaviour in a flexible way in situations that require a change in a strong habitual response or resistance to temptation (7). The abnormal interaction between reward signal processing and executive control functioning has also been related to a tendency to select immediate and appetizing (high in calories and/or sugar) rewarding choices, although these have negative consequences in the long term (8, 9). The imbalance between these two systems can be greater in adolescence, a period characterized by the relative immaturity of the prefrontal cortex, responsible for executive control, in addition to the relative maturity of striatal areas responsible for reward processing (10). Therefore, during adolescence, the activity of rewards system may prevail over that of executive control mechanisms (11).

Another factor that can impair top-down control mechanisms is stress. Stress has a harmful impact on cognitive skills, such as attention, cognitive control and decision-making, which may contribute to obesity-related behaviours in adolescents (12). Furthermore, psychosomatic theories hold that people with obesity tend to eat in response to emotional distress, showing an "emotional eating pattern" (i.e., consuming food impulsively) when under negative emotional states (13). Stress can also enhance the propensity to eat high calorie "palatable" food via its interaction with central reward pathways (14). For example, ghrelin and cortisol increase in response to social stressors and influence reward motivation, thus modulating consumption of appetizing food (15, 16)

During adolescence, peer relations are particularly salient and can serve as a robust source of distress (17). Adolescents with excess weight suffer from social stress, such as bullying or social marginalization-exclusion, more frequently than their peers (18), being subjected to frequent teasing about their body (19). Negative stereotypes toward peers with excess weight begin early in childhood (20) and these social stressors can negatively affect social adjustment and academic achievement (21). In this context, study of the detrimental influence of social stress on executive functions may be of crucial importance to understand deficient diet-related decision-making and poor emotional-regulation-related overeating in adolescents.

Several studies have found deficits in executive functioning in adults and adolescents with excess weight (22-25). However, to the best of our knowledge, no study has analyzed the influence of social stress on executive functions in adolescents with excess weight. Therefore, this study examined the effect of a social stressor on executive performance in adolescents with excess *versus* normal weight. For this purpose, the Trier Public Speaking Stress Social Task (TSST) (26, 27) was used. We analyzed the

specific influence of negative social evaluation on executive functioning and autonomic responses in adolescents with overweight. We hypothesized that excess weight adolescents would show decreased executive performance after exposure to social stress relative to normal weight adolescents. Outcome measures were working memory, cognitive inhibition, and shifting (ability to follow different rules in a task and change between them). Additionally, subjective and physiological (autonomic) indexes of stress were recorded. For this purpose, heart rate (HR) and skin conductance (SC) were continuously recorded during the TSST. Since adolescents with overweight are more often exposed to negative peer evaluations than adolescents with normal weight (18, 19), we expected greater increases in perceived stress, HR and SC in excess *versus* normal weight participants during the TSST. Furthermore, negative associations between stress-induced subjective and physiological responses and post-TSST executive performance were hypothesized.

2. Method

Participants

Sixty adolescents, 25 males and 35 females between 13 and 18 years of age, participated. They were selected based on their sex and age-adjusted BMI percentile in accordance with the guidelines of the International Obesity Task Force (IOFT) (28). Normal weight participants (n=30) had BMIs ranging between the 5^{th} and 84^{th} percentiles, and excess weight participants (n=30) had BMIs > the 85^{th} percentile. Table 1 displays the socio-demographic, BMI and body fat percentage data. Participants were recruited from high schools located in Jaén (Spain). They were screened for medical and developmental conditions, medication use, and learning disabilities. Inclusion criteria were: (i) aged range between 13 and 18 years; (ii) BMI > 5^{th} percentile; and (iii) no

history of neurological, psychiatric or eating disorders [measured using the Eating Disorder Inventory (EDI-2)]. All participants had normal or corrected-to-normal vision.

Table 1. Participants' socio-demographic characteristics, BMIs and body fat percentage.

	Excess weight		Normal weight		t[a]/chi square[b]	p
	Mean	SD	Mean	SD		
Age	15.38	1.75	15.41	1.36	-0.08[a]	0.935
Sex (%Men/ women)	46.7/53.3		36.7/63.3		0.62[b]	0.601
BMI	28.53	2.96	20.04	2.05	12.87[a]	<0.001
% Body fat	28.04	7.78	17.32	7.71	5.36[a]	<0.001

BMI body mass index.

[a]value of Student's t;

[b]value of Chi-square $\chi 2$

Executive Measures

Working memory–Letter-Number Sequencing (29): Participants were read a sequence in which letters and numbers were combined, and were asked to reproduce the sequence, first putting the numbers in ascending order and then the letters in alphabetical order. The sum of the correct answers was considered.

Inhibition and shifting–Five-digit test (FDT (30): The FDT consists of four conditions of increasing complexity. Conditions 1 and 2 evaluate processing and response speed. In condition 3 (inhibition), participants have to count the number of digits contained within various boxes, which constitutes an interference effect because the boxes contain groups of digits that do not correspond to their arithmetic value. Finally, in part 4 (shifting), participants have to count or read, depending on whether the outline of the box is normal (count, 80% of stimuli) or of double thickness (read, 20% of stimuli). The difference in performance time between part 3 and the mean of parts 1 and 2 (inhibition score), and the difference in performance time between part 4 and the mean of parts 1 and 2 (shifting score), were considered. Thus, a higher score denotes worse performance

(i.e., the participant took more time). Errors in parts 3 (inhibition) and 4 (shifting) were also analyzed.

Social stress task

To induce social stress in the laboratory, a validated Virtual Reality version of the Trier Social Stress Task (TSST-VR) was used (26). This version of the TSST was previously used in young people and has been shown to produce a significant increase in subjective stress and arousal, skin conductance and cortisol levels (27, 31). Participants had to deliver a speech about their personal characteristics, including both positive and negative aspects, in front of a simulated audience. The task is divided into two parts (each 2 min 30 s long). In the first task, the audience was interested and attentive to the speech, giving nods of understanding to the participant (i.e., positive social evaluation). In the second part, the audience began to show signs of disagreement with the speech, talking and murmuring among themselves and criticising the participant´s words (i.e., negative social evaluation). The task included four phases: a baseline rest period (3 min), delivery of the task instructions and preparation for the speech by the participant (3 m), speech during positive social evaluation, and speech during negative social evaluation. This virtual reality version of the TSST is able to induce modest but significant increases in cortisol and subjective stress responses (26).

Procedure

After obtaining permission from the high school´s directors, the study was presented to each class of students and their participation was requested. The students who were interested in taking part sent us the informed consent form, which was signed by their parents if they were minors. Then, the participants were assigned to a group and a specific day on which to complete the experimental session. Six high schools in Jaén participated in the study. The recruitment rate was approximately 4% of the total

number of students approached. Sessions started at 4 p.m. and participants were required to be satiated (having had lunch about 1 hour before) and to not have taken any caffeine. Weight and height were self-reported by participants for recruitment purposes and BMI was calculated in the laboratory, using the exact height and weight data collected on arrival. Body composition measures were also collected using the Bodystat®1500 monitoring unit. The EDI-2 (32), validated in young people, was administered to rule out eating disorders (binge eating, anorexia nervosa and bulimia nervosa). Then, executive functioning measures were conducted before TSST onset (pre-TSST) and immediately after completion of the TSST (post-TSST). The post-TSST evaluation was administered immediately after TSST. During the two evaluations, participants first completed the Letter-Number Sequencing and then the Five Digit Test. Subjective stress was measured by a visual analogue scale (VAS, ranging from 1 to 10; no stress to extreme stress) before and after exposure to TSST. The virtual reality TSST was carried out in a soundproof room, with white walls and without any distracting stimuli. The equipment consisted of a computer running the program containing the social scenes, and a projector for their display on the wall. Previous validation studies indicated increases in skin conductance and salivary cortisol during the task, both when scenes were presented via goggles or projected on to a screen (31). However, participants rated task immersion as being higher with the wall-screen presentation versus the goggles (31). Surround-sound headphones were used to allow perception of the sound emanating from the room where the audience was situated, and the murmurs and comments of the listeners. The Ethics Committee of the Universidad de Jaén approved the study. Both participants and parents signed informed consent forms.

Psychophysiological Data Acquisition and Processing

HR and SC were continuously recorded during the TSST using a Biopac MP150 polygraph (Biopac Systems Inc., USA). HR (beats per minute) was derived from an electrocardiogram (ECG) recorded at 1000 Hz. ECG electrodes (Ag/AgCl) were attached to the participant's right mid-clavicle and the lowest left rib (left wrist as the ground). HR was extracted from ECG recordings using the software AcqKnowledge 3.9.1 (Biopac Systems Inc.) and edited for artifacts (when present) via linear interpolation. SC (micro-Siemens, μS) was recorded at a sampling rate of 500 Hz using Ag–AgCl electrodes filled with an inert 0.05 M NaCl electrolyte cream and attached to the palmar surface of the second and third middle phalanges of the participant's non-dominant hand. Two participants (one from each group) had unusable SC recordings.

Statistical analyses

Group comparisons were carried out with Student's *t*-test for independent samples. Responses to the TSST were analyzed by repeated measures ANOVA with Time (pre- and post-TSST) as the repeated-measures factor and Group (Excess versus Normal weight) as the between-subject factor. Although the TSST consisted of four phases, given our specific interest in the effect of social evaluation, HR and SC analyses were restricted to the difference between the latter two parts of the TSST involving social evaluation (positive *versus* negative social evaluation). Associations between variables were analyzed by Pearson's correlations. To simplify the correlation analysis, change scores were computed as the difference between the post- and pre-TSST values.

3. Results

Associations between measures

In the whole sample, the change in HR was positively associated with changes in stress VAS scores (r=0.32, p=0.013), "shifting errors" (r=0.30, p=0.02), "inhibition errors"

(r=0.38, p=0.003) and the "shifting score" (r=0.26; p=0.046). The change in SC correlated inversely with the change in Letter-Number Sequencing (r=-0.33, p=0.01), and positively with the change in stress VAS scores (r=0.26, p=0.047). Finally, the change in stress VAS scores correlated positively with the change in "inhibition errors" (r=0.46, p<0.001). BMI was positively associated with post-TSST "inhibition errors" (r=0.51, p<0.001), "shifting errors" (r=0.32, p=0.001) and stress VAS scores (r=0.31, p=0.015).

Subjective stress

A Time x Group interaction was found for stress VAS scores ($F_{1,58}$=9.76, p=0.003, η_p^2=0.14). While in adolescents with excess weight stress levels increased from pre- to post-TSST evaluation ($F_{1,29}$= 65.89, p<0.001, η_p^2=0.69), the change in adolescents with normal weight did not reach significance ($F_{1,29}$=2.66, p=0.115, η_p^2=0.08) (Table 2).

Table 2. Descriptive scores and group comparisons for stress (VAS) and neuropsychological measures before TSST (PRE-scores) and after TSST (POST-scores)

	Excess weight		Normal weight		t	p	*d´*
	Mean	SD	Mean	SD			
Stress Pre	1.49	1.65	1.82	1.91	0.72	0.474	0.18
Stress Post	4.03	2.45	2.59	2.18	2.39	0.020	0.62
Letter-Number Sequence Pre	9.03	2.53	8.73	1.76	0.53	0.597	0.14
Letter-Number Sequence Post	9.03	2.93	10.87	2.70	2.52	0.015	0.65
Score-inhibition-5DigitTest Pre	17.13	7.16	13.75	5.33	2.07	0.042	0.54
Score-inhibition-5DigitTest Post	12.73	4.40	10.85	5.16	1.52	0.134	0.39
Score-shifting-5DigitTest Pre	22.37	6.80	20.81	5.99	0.94	0.353	0.24
Score-shifting-5DigitTest Post	21.07	3.86	16.52	4.84	4.02	<0.001	1.04
Errors-inhibition-5DigitTest Pre	0.77	0,97	0.70	0.95	0.27	0.067	0.01
Errors-inhibition-5DigitTest Post	1.70	0.95	0.37	0.61	6.44	<0.001	1.67
Errors-shifting-5DigitTest Pre	1.50	1.57	1.13	1.25	1.00	0.321	0.26
Errors-shifting-5DigitTest Post	2.37	2.35	0.80	1.29	3,19	0.002	0.83

VAS visual analogue scale; *TSST* Trier Social Stress Task; *FDT* Five-Digit Test.

Psychophysiological measures

No group differences were found in HR or SC during the pre-TSST evaluation. A Time x Group interaction was found for HR ($F_{1,58}$=8.26, p=0.006, η_p^2= 0.13) (Figure 1). While HR increased in adolescents with excess weight from the positive to the negative social evaluation phase of TSST ($F_{1,29}$=8.45, p=0.007, η_p^2=0.23), no change was observed in adolescents with normal weight ($F_{1,29}$=1.16, p=0.29, η_p^2=0.04). A Time x Group interaction was also observed in SC ($F_{1,56}$=4.76, p=0.033, η_p^2=0.08) (Figure 2). While SC decreased in adolescents with normal weight from the positive to the negative social evaluation phase of the TSST ($F_{1,28}$=17.15, p<0.001, η_p^2=0.38), no change was observed in adolescents with excess weight ($F_{1,28}$=0.24, p=0.63, η_p^2=0.01).

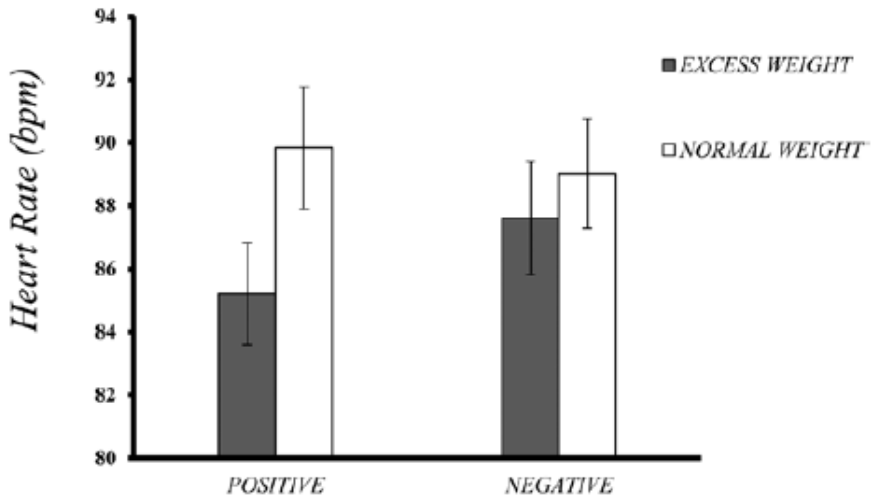

Fig. 1. Mean heart rate (beats per minute [BPM]) during the positive and negative social evaluation phases of the Trier Social Stress Task. Bars indicate standard error of the mean.

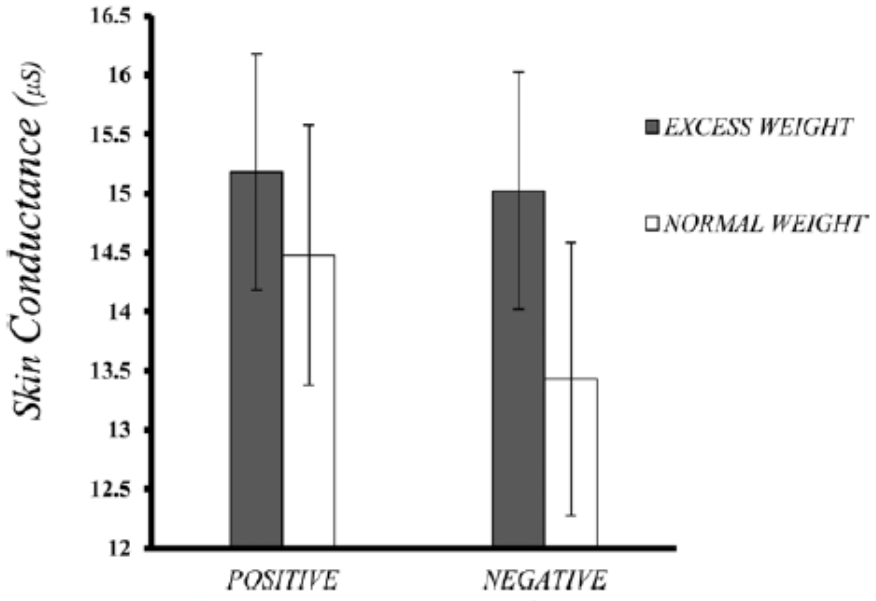

Fig. 2. Mean skin conductance (micro-Siemens) during the positive and negative social evaluation phases of the Trier Social Stress Task. Bars indicate standard error of the mean.

Executive functions

During the pre-TSST evaluation, excess weight participants showed greater scores in the inhibition condition of FDT (i.e., lower inhibition) than normal-weight participants ($t=2.08$, $p=0.042$, $\delta=0.54$). No other significant differences arose during pre-TSST (see Table 1). Significant Time x Group interactions were found for Letter-Number Sequencing ($F_{1,58}=16.82$, $p<0.001$, $\eta_p^2=0.23$) (Figure 3), "inhibition errors" in FDT ($F_{1,58}=31.34$, $p<0.001$, $\eta_p^2=0.35$), "shifting errors" in FDT ($F_{1,58}=10.80$, $p=0.024$, $\eta_p^2=0.08$) (Figure 4) and "shifting score" in FDT ($F_{1,58}=15.47$, $p=0.039$, $\eta_p^2=0.07$). Adolescents with normal weight significantly increased their performance after the TSST in Letter-Number Sequencing ($F_{1,29}=26.14$, $p<0.001$, $\eta_p^2=0.47$) and "shifting score" ($F_{1,29}=23.02$, $p<0.001$, $\eta_p^2=0.44$) and decreased their "inhibition errors" (FDT) ($F_{1,29}=6.59$, $p=0.01$, $\eta_p^2=0.19$). By contrast, adolescents with excess weight increased

their "inhibition errors" (FDT) ($F_{1,29}$=25.38, p<0.001, η_p^2=0.467) and, marginally, their "shifting errors" (FDT) ($F_{1,29}$=4.15, p=0.051, η_p^2=0.13).

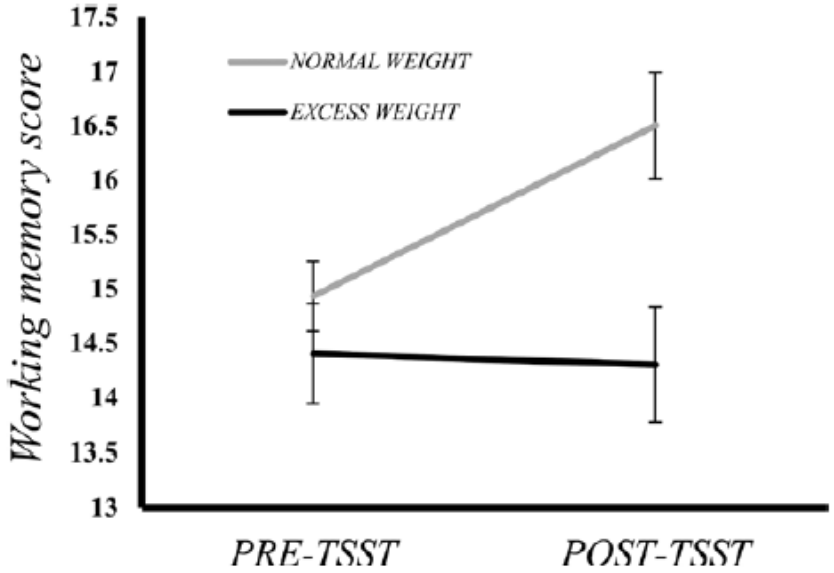

Fig. 3. Working memory scores (Letter-Number Sequencing) before and after the Trier Social Stress Task. Bars indicate standard error of the mean.

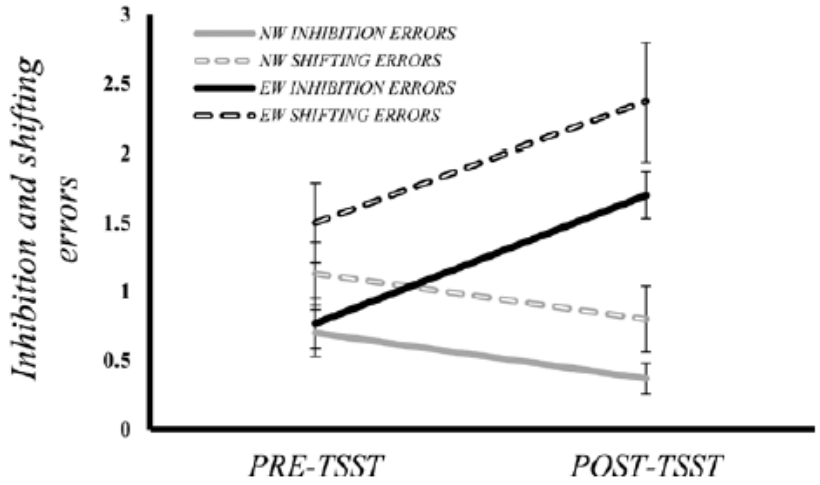

Fig. 4. Inhibition and shifting errors (Five Digit Test) before and after the Trier Social Stress Task in normal weight (NW) and excess weight (EW) adolescents. Bars indicate standard error of the mean.

4. Discussion

Adolescents with excess weight, compared to those of normal weight, showed impairments in measures of inhibition and shifting, and higher subjective stress levels,

in response to the TSST. Furthermore, adolescents with excess weight showed a differential psychophysiological pattern during the TSST. HR increased during the negative social evaluation phase (relative to the positive phase) in this group, while no change was observed in adolescents with normal weight. SC decreased in adolescents with normal weight from the positive to the negative social evaluation phase, suggesting habituation to the situation, but did not change in adolescents with excess weight. Skin conductance is a variable that usually displays a decrease over the recording period, denoting habituation to the situation. A flat recording, without any sign of decrease, is usually interpreted as indicating a high electrodermal level (33).

Our findings suggest that adolescents with overweight-obesity have enhanced sensitivity to social stressors. This is manifested both at subjective and physiological levels. Subjectively, the greater increase in stress levels indicates that adolescents with excess weight perceive the situation as more stressful than do adolescents with normal weight. At the physiological level, results indicate a greater mobilization of physiological resources and autonomic reactivity during social stress, particularly during negative social evaluation, in adolescents with excess weight. The most common motivation for using a public speaking task is that it elicits a social evaluation-related threat (34). The inclusion of the two phases of the TSST as a function of feedback from the audience (positive *versus* negative) allowed for a more specific analysis of social evaluation, making our results more innovative. Taken together, these results support the utility of differentiating between positive versus negative social evaluation during the TSST for the study of the impact of social stress on autonomic and cognitive functions.

The observed negative impact of social stress on executive functioning in adolescents with excess weight is consistent with a previous study which showed impaired attention

after TSST in adolescents with excess weight compared to adolescents with normal weight (27). Negative emotional states in adults are known to impair cognitive capacity; for example, depressive symptoms in people with obesity impair executive function (35). Furthermore, emotional eating patterns, which are more prevalent in this population (15), may additionally affect executive functioning. Specifically, socially stressful situations evoke negative mood states and impair impulse control. The joint influence of executive deficits and emotional eating patterns would lead to further eating disinhibition. However, no previous studies have analyzed the effects of emotional states on executive functioning in adolescents with excess weight.

Inhibition, shifting and working memory were negatively affected by social stress in our excess weight adolescents. This suggests that social stress has a detrimental impact on executive functioning in these adolescents, and this may influence their eating behaviour. Usually, in pre-post cognitive evaluations, performance improves in the second evaluation due to practice effects arising from repeated administration (36, 37). In fact, in this study working memory improved significantly in the normal weight group from the pre- to post- TSST evaluation. However, adolescents with excess weight did not benefit from this learning experience, and in fact their performance decreased. A previous study (27) using the same experimental protocol also found increases in attention performance in normal weight participants from the pre- to post-TSST evaluation, while excess weight participants were unable to benefit from the practice effect. These results may be due to the greater levels of stress during the TSST in adolescents with excess weight. Stress negatively affects abilities that require conscious attention and effortful information processing, reducing therefore cognitive efficiency (38). Greater cortisol responses to the TSST were found in the previous study (27), and results of the present study showed higher heart rate and electrodermal reactivity to the

social stress task in adolescents with excess weight. Furthermore, autonomic reactivity after TSST, specifically electrodermal response, correlated inversely with working memory performance in the whole sample. Therefore, the greater autonomic and stress response in adolescents with excess weight can increase stress interference in this group and therefore lead to a deficit in learning from the repeated administration of the tasks.

Executive functioning may have multiple direct and indirect influences on obesity in adolescence. Although available evidence links executive functioning and obesity (24, 39), the specific mechanisms mediating this association are less well-known. Some studies have found that executive dysfunction is associated with obesity-related behaviours in childhood and adolescence via increasing intake, disinhibiting eating, and reducing physical activity. The inability to inhibit impulses predicted higher food intake, a higher body weight and less weight loss after a weight reduction intervention (40). Deficits in inhibition can impact impulse control and thus the capacity to restrict intake of appetizing foods (high fat/sugar). Impairments in shifting may influence the capacity to regulate and modify eating behaviours in order to prevent harmful health consequences. Furthermore, this deficit may lead to adolescents with excess weight persisting in their unhealthy eating habits. Impairments in working memory could affect the ability to maintain cognitive control, making it more difficult to engage in healthy activities and intervention programs. Finally, disinhibited eating in obese adolescents was associated with reduced orbitofrontal volume and executive dysfunctions, which were most pronounced in terms of working memory and inhibition (41). Conversely, executive function skills were positively associated with healthy eating habits, such as fruit and vegetable intake, and physical activity (42, 43).

We observed group differences before social stress only in the “inhibition score” (FDT), with lower performance in excess than normal weight adolescents. However, no

differences were found in shifting or working memory. These results are concordant with a previous study reporting selective alterations in inhibition in adolescents with obesity versus normal weight adolescents (43). Another study found selective alterations in inhibition and shifting, but not working memory, in excess weight and obese adolescents (24). In contrast, others authors found significant differences between obese and normal adolescents in working memory as well as attention, but not in intelligence or verbal fluency (44). Discrepancies between studies may be due to differences in testing methods, samples and levels of BMI.

As expected, the change in subjective stress was positively associated with the change in HR, SC and "inhibition errors" (FDT). This suggests that levels of subjective stress may modulate both psychophysiological responses and executive-inhibition functions. In this way, negative social evaluations may induce a greater increase in stress levels and autonomic responsiveness, and a reduction of inhibition capacity, in excess weight adolescents relative to those with normal weight. The deleterious influence of negative social evaluation on executive control in adolescents with excess weight may exacerbate difficulties in eating behaviour control, eventually triggering overconsumption.

The change in HR during social evaluation was positively associated with the change in "shifting errors", "inhibition errors" and "shifting score" in the whole sample. The change in SC was negatively associated with the change in Letter-Number Sequencing performance (i.e., greater habituation of skin conductance was associated with better working memory). These results suggest that modulation of autonomic activity by social stress may index, or additionally influence, executive functioning in adolescents with excess weight. This harmful effect on executive functioning may lead to problems in real life, such as poor regulation of eating habits. However, studies in adults also using the TSST did not find differences in HR, blood pressure or cortisol responses

between obese and normal weight individuals (15). This discrepancy may be due to the non-inclusion of specific positive-negative evaluation phases in their TSST, or may reflect a greater vulnerability to social stress in adolescents than adults. In line with the greater autonomic response found in our study, a greater cortisol response after the TSST has been previously found in excess weight than in adolescents with normal weight (27).

Executive functioning is still developing during adolescence, since prefrontal areas reach full development at maturity (45). A growing body of literature suggests an altered balance between the earlier-developing limbic system and the later developing frontal/executive system (46) during adolescence. Furthermore, in this period, the opinions of peers and general social evaluation become a central aspect for self-image development (47). Adolescents with excess weight frequently suffer from negative social evaluations and social stressors during their everyday lives, which may lead to greater vulnerability to social stress, especially if a negative social evaluation component is included. It would be reasonable to assume that adolescents with excess weight would show a blunted stress response due to habituation to repeated stress exposure. However, previous studies using this same TSST protocol found greater increases in salivary cortisol in excess weight than in normal weight adolescents (27). These results suggest the development of a sensitization process to social stress in adolescents with excess weight.

Therefore, due to all of the factors listed above, adolescents with excess weight are an important target group for cognitive interventions based on stress regulation strategies, executive function improvement and prevention of harmful eating behaviours. In this regard, some evidence already suggests that executive functioning training for obese

children can improve working memory, inhibition and shifting, being useful in weight-loss maintenance (48).

Regarding its strengths, our study used an innovative strategy to evaluate the impact of social stress, particularly negative social evaluation, on adolescents with excess weight, as well as the inclusion of autonomic variables as objective indices of stress. Among the limitations, we used a virtual reality audience in our TSST instead of the actual public, which might have decreased the realism of the situation and the stress-elicited responses. However, this version of the TSST was validated in previous studies and produced a reliable stress response (26, 27, 31). Furthermore, the inclusion in future studies of a non-stress control condition (also with two cognitive evaluations) is recommended to rule out more possible general disruption of cognitive processes in excess weight adolescents. Regarding the study design, the absence of any counterbalancing of the order of presentation of positive versus negative feedback conditions might have influenced the results. Therefore, this aspect should be taken into account in future studies. Additionally, we did not assess factors like emotional eating or loss of control in eating behaviour, which may be relevant to overeating. Finally, longitudinal studies are necessary to better analyse the influence of stress-induced executive functioning decrements on the propensity to overeat and become obese in the future in adolescents with excess weight.

In summary, our results showed a harmful impact of social stress, specifically negative social evaluation, on executive functioning of adolescents with excess weight. Adolescents with overweight performed worse after TSST in inhibition and shifting than those with normal weight, and they did not benefit from learning in the domain of working memory, in contrast to adolescents with normal weight. Furthermore, in association with the observed decreases in neuropsychological performance, adolescents

with excess weight showed greater subjective and autonomic stress responses to negative social evaluation. Given the relevance of high order executive functions to self-control of eating behaviour (49, 50), the results presented herein highlight the value of assessing the social evaluation context, and how it may be associated with differential changes in cognitive functioning in adolescents with overweight. This stress-mediated impairment in cognitive functioning could increase the risk for future obesity. Interventions aimed at social stress coping strategies and improvement of executive functions could be useful in the prevention of obesity in adulthood.

Authors' Statement of Conflict of Interest. The authors declare no conflicts of interest.

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<u>Capítulo 8.</u> Risky decision-making after exposure to a food-choice task in excess weight adolescents: relationships with high-calorie food preferences and hunger

Moreno-Padilla, M., Fernández-Serrano, M. J., & Reyes del Paso, G. A. (2018). Risky decision-making after exposure to a food-choice task in excess weight adolescents: Relationships with reward-related impulsivity and hunger. *PloS one, 13*(8), e0202994. doi: 10.1371/journal.pone.0202994

1. Introduction

The prevalence of overweight and obesity in adolescence has increased considerably in recent decades [1,2]. Excess weight in adolescents is a strong predictor of adult obesity [3]. Overweight and obesity, being associated with increased incidence rates of diabetes, cardiovascular diseases and certain kinds of cancer, are currently the fifth-leading mortality risk factor (World Health Organization [WHO]).

In the last few decades, drastic changes in the environment and lifestyles have modified the way we perceive foods and regulate their intake [4]. The availability of a wide range of foods, and overexposure to marketing-related images of foods in Western societies, has led to what, and how much, to eat becoming a decision-making matter. Obesity has been proposed as a problem of food addiction, with overeating explained as an imbalance between motivational and control-inhibition systems [5,6]. From this theory, it is proposed that in vulnerable individuals, the consumption of large amounts of appetizing food (high in fat and/or sugar) could cause an imbalance in the interaction of these systems, resulting in an increase in the motivational-reinforcing value of appetizing food and a weakening of the control-inhibitory system [6]. This deficit in control and inhibitory influences would lead to impulsive and compulsive intake of appetizing foods, and as a consequence, to the development and maintenance of obesity [6].

The impact of inhibitory control on eating behaviour seems to be particularly relevant during adolescence [7], a developmental period in which both motivational tendencies and impulse control skills strongly modulate goal-directed behaviour [8]. Furthermore, decision-making skills are particularly relevant in adolescents, in whom executive

control areas (prefrontal areas) are not completely developed and seem to maximize reward at the expense of risk [8].

A relevant perspective in impulsive decision-making is the concept of risk-taking. Risk-taking propensity refers to the appetitive processes underlying a behavioral predisposition to take risks in response to signals for potential reward, which also confers a probability of unattractive results [9]. In recent years, the concept of risk-taking has been used to describe impulsive behavior in drug addiction and obesity [10,11]. Previous studies have repeatedly shown that drug abusers are risk prone, as evidenced by self-reports of sensation seeking [12] and behavior in laboratory risk-taking tasks [13]. Obesity is also associated with greater risk-taking, showing an association with risky patterns of responses in tasks like the Iowa Gambling Task (IGT) [14].

Adolescents are known to have a tendency to take more and greater risks than individuals in other age ranges in many life domains, such as unprotected sex, criminal behavior, dangerous driving, and experimenting with alcohol and other drugs [15]. Furthermore, adolescents who are reward sensitive and have difficulties in controlling their behavior appear to be most susceptible to involvement in risky behavior [16].

There is increasing evidence that individual differences in the tendency to overeat are related to impulsivity, possibly due to increasing reactivity to environmental food-related cues [17]. Neurocognitive studies have shown that obesity and addiction are both associated with increased impulsive decision-making and attentional bias in response to drug or food cues, respectively [18]. Several studies have analyzed attentional bias in individuals with obesity, but the results have been inconsistent [19,20]. When participants were tested in a hungry state, no differences were found, but

when they were satiated at the time of testing, greater attentional bias was found in excess compared to normal weight adults [21]. However, specific literature on adolescents is scarce. To the best of our knowledge, only one study has found increased attentional bias and impulsivity to food cues in adolescent girls, as well as reduced activation of frontal inhibitory regions [22].

Regarding appetitive motivation, substance use disorders (addiction) and obesity, and subjective states of craving and hunger, are associated with attentional bias for drug- and food-related stimuli, respectively [23,24]. Furthermore, previous studies showed that drug-cue reactivity is positively associated with increases in impulsivity and risk-taking in substance abusers [25].

Decision making in eating behaviour can be studied by food choices tasks. Food decisions concern what, when, and how much to eat. Food choices can lead to overconsumption, when there is an increased preference for appetizing food (high in fat and/or sugar). Therefore, the study of decision making is extremely important in this population, since decision making based in unhealthy choices can lead to weight more gain and develop or maintain obesity.

This study examined the effect of exposure to food pictures, in a food-choice task, on subsequent measures of risky decision-making and hunger levels in adolescents with excess *versus* normal weight. Risk seeking was assessed through the Balloon Analogue Risk Task (BART). Riskiness on the BART was related to self-reported engagement in real-world risk-taking behaviours [26]. To study the influence of exposure to food pictures, performance on the BART and feelings of hunger were evaluated both before and after the food choice task. We hypothesized that adolescents with excess weight would show greater risky decision-making after exposure to food pictures, while no

change was expected in normal weight adolescents. We expected to find greater increases in hunger levels after the food-choice task in excess *versus* normal weight participants. Finally, we expected to find more food-appetizing choices among excess weight adolescents, as well as associations between impulsivity measures, hunger levels and risk-taking outcomes.

2. Methods

Participants

In total, 56 adolescents (24 males and 32 females) aged between 13 and 18 years participated in the study. They were selected based on their age adjusted body mass index (BMI) percentile in accordance with the guidelines of the International Obesity Task Force [27] criteria: normal weight participants (n=29), with age-adjusted BMI values in the range between the 5th and the 84th percentile, and excess weight participants (n=27), with age adjusted BMI values above the 85th percentile. However, the participant of higher weight in the normal weight group has a percentile of 70. Socio-demographic, BMI, waist-hip ratio and fat percentage data are displayed in Table 1. Participants were recruited from high schools located in Jaén (Spain). The inclusion criteria were: (i) aged between 13 and 18 years; and (ii) no history of neurological or psychiatric disorders. All participants had normal or corrected-to-normal vision.

Table 1. Participants' socio-demographic characteristics, BMI, percentage of body fat and waist-hip ratio.

	Excess weight		Normal weight		t[a]/chi square[b]	p
	Mean	SD	Mean	SD		
Age	15.28	1.82	15.43	1.39	-0.36[a]	0.723
Sex (%Men/women)	46.7/53.3		36.7/63.3		1.72[b]	0.189
BMI	28.33	2.74	20.12	2.05	12.76[a]	<0.001
Waist-Hip ratio	0.85	0.05	0.82	0.07	1.69 [a]	0.097
% Body fat	27.34	7.71	17.90	7.16	4.75[a]	<0.001

[a]value of Student's t;
[b]value of Chi-square $\chi 2$

Instruments

Self-reported measures

- Spanish version of the short UPPS-P impulsive behavior scale [28]: the UPPS-P is a 20-item inventory designed to measure five components of impulsive behavior: sensation seeking, lack of perseverance, lack of premeditation and urgency (positive and negative). Each item on the UPPS-P is rated on a four-point scale ranging from 1 (strongly agree) to 4 (strongly disagree). Positive Urgency is defined as the tendency to act rashly to obtain reinforcement when experiencing positive emotions, while Negative Urgency refers to the tendency to engage in impulsive behaviours under conditions of negative affect. Sensation seeking describes individuals' tendency to seek out novel, complex, and intense sensations and experiences, and a predisposition to take risks to realise these experiences. Lack of Premeditation refers to the tendency to think and reflect on the consequences of an act before engaging in that act or taking a decision. Lack of Perseverance refers to an individual's inability to remain focused on a task that may be boring or difficult.
- A visual analogue scale (VAS) designed to rate hunger levels. Participants had to indicate how hungry they were feeling on a scale ranging from 1 to 10 (not hungry to very hungry).

Risk-taking task

The BART [29] is a 20-trial computerized task that models real-world risk behavior according to the concept of balancing the potential for reward and harm [29]. The participant is presented with a balloon and asked to pump it up by clicking a button on the screen. With each pump, the participant obtains 25 cents and the balloon increases slightly in size. However, each balloon also has a concealed probability of exploding after an unspecified number of pumps. Participants were told that at some point each

balloon would burst. Before the balloon explodes, the participant can press "Collect money," which saves his or her earnings to a permanent bank. If the balloon explodes before the participant collects the money, all earnings for that balloon are lost, and the next balloon is presented. Each successful click increases the participants' temporary payoff but increases the risk of the balloon exploding. Thus, each pump confers not only greater risk but also greater potential reward.

In this version of the task, the maximum number of pumps possible for a given balloon was 128, thus the probability of the balloon exploding on Pump 1 was 1/128. If there was no explosion after this first pump, the probability of explosion on Pump 2 was 1/127, and so on up until the 128th pump. Accordingly, the average break point or "optimal stopping point" for each balloon was 64 pumps.

Dependent variables are the average number of pumps of unexploded balloons and the number of exploded balloons (higher scores indicate greater risk-taking propensity).

Food-choice task

A food preference decision-making task was used in this study. Two types of food pictures were utilized: appetizing (high levels of fats and/or sugars) and healthy. Appetizing cues included, for instance, sausages and chocolate and healthy cues included, for instance, fruits and salads. In each trial, pairs of pictures of these different types of foods were presented in three conditions (appetizing vs. healthy, appetizing vs. appetizing and healthy vs. healthy). Participants had to choose between the two options by pressing a computer keyboard. Each trial begins with a fixation cross which lasts from 3 to 6 seconds, varying between trials. Then, the images of the two options appear for 5 seconds (one on the left side of the screen and the other one on the right side of screen, with the positions of the appetizing and healthy foods varying among trials). The order of presentation of the images was counterbalanced across the participants. Then,

the fixation cross was represented. There were a total of 30 choice trials, with 10 choices for each decision category, preceded by four practice trials. The outcome measure was the number of selections of each type of food.

Procedure

Height, weight and body composition measures (Bodystat®1500 monitoring unit) were collected on arrival of the participant. Subsequently, the UPPS-P impulsivity questionnaire was administered followed by the BART (pre-task). Then, participants performed the food-choice task, and immediately after, the BART was administrated again (post-task). Subjective hunger evaluation (VAS) was carried out before (and after UPPS-P) (pre-task) and after completion of the food-choice task (post-task). The Ethics Committee for Human Research of the Universidad de Jaén approved the study. Both participants and parents signed informed consent forms.

Statistical analyses

Group comparisons were carried out with Student *t*-test for independent samples. BART and hunger measures were analyzed by repeated measures ANOVA with Time (pre- and post-task) as the repeated-measures factor and Group (Excess vs. Normal weight) as the between-subject factor. Additionally, we have carried out ANCOVA analyses including the covariables of Sensation Seeking and Positive Urgency in order to assess the influence of these variables on the pre- to post- change. Associations between variables were analyzed by Pearson correlations. Finally, mediation analyses were performed with the PROCESS macro for SPSS. To assess the significance of partial mediation effects, confidence intervals from the bootstrapping estimation techniques were used. For a significant meditational effect, the limits of confidence interval should not include the 0 value [30, 31]. In order to simplify these analyses, change scores were calculated as the post-task value minus the pre-task value.

3. Results

Self-reported measures

The groups differed in two dimensions of the impulsivity questionnaire (UPPS-P), sensation seeking (t=2.17, p=0.034, δ=0.58) and positive urgency (t=2.14, p= 0.037, δ=0.56), with greater scores in the excess *versus* normal weight adolescents (Table 2). A Time x Group interaction was found for hunger VAS scores ($F_{1,54}$ = 8.56, p =0.005, η_p^2=0.14). Although both groups showed significant increased hunger levels, the increase from the pre- to post-task evaluation was greater in excess weight ($F_{1,26}$= 33.72, p<0.001, η_p^2=0.57) *versus* normal weight adolescents ($F_{1,28}$=17.37, p< 0.001, η_p^2=0.38) (Table 2).

Additionally, results of ANCOVA showed that Sensation Seeking had a significant effect on the change in hunger levels in the whole sample (F1,53= 4.13, p=0.047, η_p^2=0.072). Furthermore, a Sensation Seeking x group x time (F1,53= 8.40, p=0.001, η_p^2=0.241) interaction was found. In order to analyze this interaction we explored the effect of the covariable in each group separately. Sensation Seeking influenced the change in hunger levels in the excess weight group (F1,25 = 7.97, p=0.009, η_p^2=0.242), but not in the normal weight group (F1,27= 0.03, p=0.869, η_p^2=0.001). Regarding food choices, excess weight adolescents chose significantly more appetizing foods than normal weight adolescents (Table 2).

Table 2. Means and standard deviations (SD) of impulsivity (UPPS-P), hunger (VAS) measures, appetizing and healthy choices. Results of the group comparisons (t and p) are also displayed.

	Excess weight		Normal weight		t	p
	Mean	SD	Mean	SD		
UPPS-P Urg-	11.89	8.65	10.90	3.44	0.57	0.570
UPPS-P Urg+	9.96	2.12	8.86	1.73	2.14	0.037
UPPS-P SS	11.19	2.63	9.62	2.74	2.17	0.034
UPPS-P LPrem	8.37	1.94	8.24	2.59	0.21	0.835
UPPS-P LPers	7.63	2.10	8.31	2.56	-1.08	0.284
UPPS-P Total	46.04	9.63	47.03	8.09	-0.42	0.676
Hunger Pre	1.35	1.48	2.35	2.26	-1.94	0.057
Hunger Post	4.94	2.62	3.88	2.77	1.48	0.144
A_Choices	7.11	2.06	4.38	2.53	4.41	<0.001
H_Choices	2.89	2.06	5.62	2.53	-4.41	<0.001

Note: Urg-: Negative Urgency; Urg+: Positive Urgency; SS: Sensation Seeking; LPrem: Lack of Premeditation; LPers: Lack of Perseverance; A_Choices: appetizing choices; H_Choices: healthy choices

Risk-taking task (BART)

Significant Time x Group interactions were found for the average number of pumps of unexploded balloons ($F_{1,54}$= 5.68, p=0.021, η_p^2=0.10) (Fig 1) and exploded balloons ($F_{1,54}$= 7.38, p=0.009, η_p^2=0.12) (Fig 2). The average number of pumps of unexploded balloons ($F_{1,26}$= 14.57, p=0.001, η_p^2=0.36) and exploded balloons ($F_{1,26}$= 6.33, p=0.018, η_p^2=0.20) increased in excess weight adolescents after the food-choice task, while no significant changes were observed in normal weight adolescents (p>0.23). While no group differences in the BART were observed in the pre-task evaluation (exploded balloons: p=0.855; average number of pumps on unexploded balloons: p=0.702), the above-described differential responses to the food choice task led to increased risk-taking (exploded balloons) in the excess *versus* normal weight adolescents during the post-task evaluation (t=2.43;p=0.019; δ =0.67).

The inclusion of Sensation Seeking and Positive Urgency as covariables in these analyses did not change the above results.

Fig 1. Average Number of Pumps on Unexploded Balloons in the Pre-Task and Post-Task evaluations as a function of group.

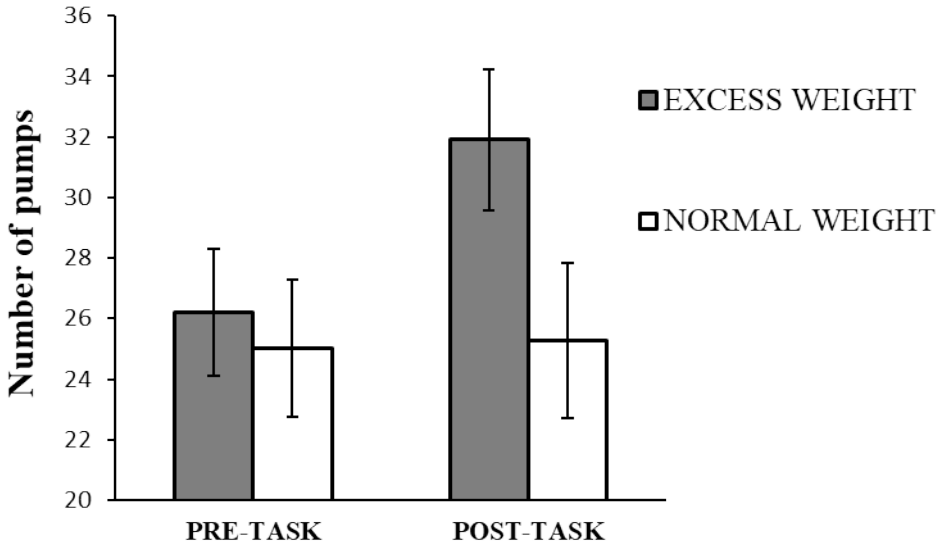
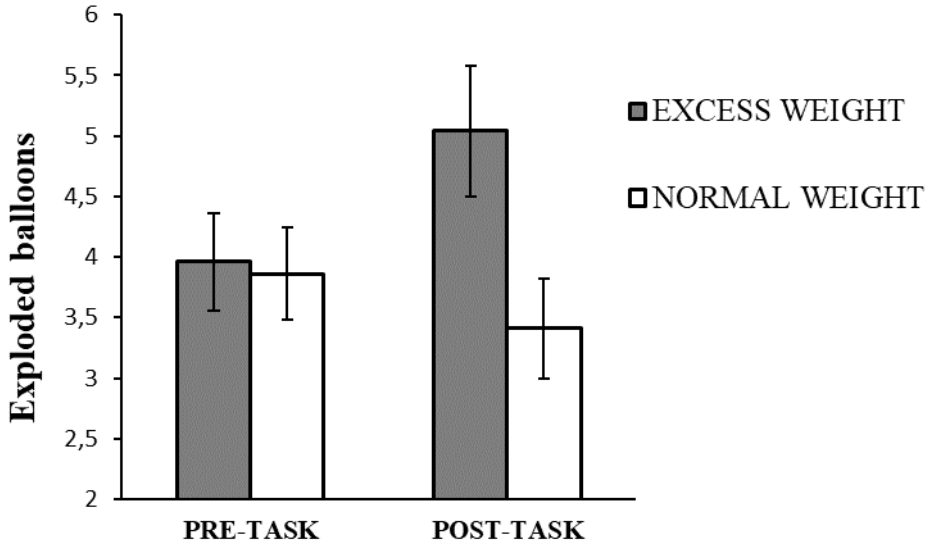


Fig 2. Number of Exploded Balloons in the Pre-Task and Post-Task evaluations as a function of group.



Associations between measures

In the whole sample (Table 3), the change in hunger levels was positively associated with the change in the number of exploded balloons, the number of exploded balloons after the food-choice task and the average number of pumps on unexploded balloons

before and after the food-choice task. Sensation Seeking was positively associated with the change in hunger levels, the number of appetizing choices made in the food choice task, the number of exploded balloons and the average number of pumps on unexploded balloons after the food-choice task. Positive Urgency, Lack of Perseverance and UPPS-P total scores were positively correlated with the number of appetizing choices. Finally, BMI was positively associated with the change in the number of exploded balloons, the number of exploded balloons after the food-choice task, Positive Urgency, Sensation Seeking and the number of appetizing choices.

In the excess weight group (Table 4), the change in hunger levels was positively associated with the change in the number of exploded balloons, the number of exploded balloons after the food-choice task, the average number of pumps on unexploded balloons before and after the food-choice task and sensation seeking scores. Sensation Seeking was positively associated with the number of exploded balloons after the food choice task. UPPS-P total scores were correlated with the number of appetizing choices. Finally, Lack of Perseverance was positively associated with BMI and the number of exploded balloons before the food choice task. In the normal weight group (Table 5), Negative Urgency, Lack of Perseverance and UPPS-P Total scores correlated positively with the number of appetizing choices. Finally, BMI was positively associated with Lack of Premeditation.

Results of mediation analysis showed that the change in hunger levels mediated the difference in the number of exploded balloons between the pre- and post-administrations of the BART in excess weight participants (Bootstrapping Lower Limit Confidence Interval = 0.04, Bootstrapping Upper Limit Confidence Interval = 0.54), and not in normal weight participants (Bootstrapping Lower Limit Confidence Interval = -0.14, Bootstrapping Upper Limit Confidence Interval = 0.06).

Table 3. Pearson correlations between variables in the whole sample are displayed.

n=56	Hunger_ Change	UPPSP_ T	UPPSP_ U+	UPPSP_ U-	UPPSP_ SS	UPPSP_ LPrem	UPPSP_ LPers	BMI
Hunger_change	1	0.05	0.03	-0.00	0.34*	0.01	-0.17	0.25
EB_Change	0.33*	-0.13	-0.08	-0.03	0.23	-0.04	-0.16	0.30*
ANPUB_Change	0.08	-0.20	0.09	0.10	0.17	-0.06	-0.22	0.18
EB_PRE	0.20	0.16	0.06	0.22	0.22	0.06	0.25	0.09
EB_POST	0.43**	0.01	-0.02	0.15	0.37**	0.01	0.06	0.33*
ANPUB_PRE	0.28*	0.14	-0.06	0.00	0.18	0.02	0.18	0.11
ANPUB_POST	0.34*	-0.06	0.02	0.12	0.28*	-0.04	-0.04	0.22
A_Choices	0.24	0.42**	0.36**	0.07	0.27*	0.25	0.29*	0.45**
BMI	0.25	0.04	0.33*	0.09	0.27*	0.16	0.01	1

EB: Exploited Balloons; ANPUB: Average Number of Pumps on Unexploded Balloons; T: total; U+: Positive Urgency; U-: Negative Urgency; SS: Sensation Seeking; LPrem: lack of premeditation; LPers: lack of perseverance; A_Choices: appetizing choices; BMI: Body Mass Index

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

Table 4. Pearson correlations between variables in excess weight group are displayed.

n=29 Normal weight	Hunger_ Change	UPPSP_ T	UPPSP_ U+	UPPSP_ U-	UPPSP_ SS	UPPSP_ LPrem	UPPSP_ LPers	BMI
Hunger_change	1	-0.04	-0.03	0.03	-0.03	-0.08	-0.18	0.14
EB_Change	-0.14	-0.30	-0.25	-0.28	0.13	-0.15	-0.06	-0.07
ANPUB_Change	-0.27	-0.19	-0.14	-0.17	0.29	-0.15	-0.19	-0.24
EB_PRE	0.03	0.27	0.04	0.18	0.07	-0.01	0.13	0.32
EB_POST	-0.10	-0.02	-0.19	-0.09	0.19	-0.14	0.06	0.24
ANPUB_PRE	0.10	0.04	-0.14	-0.07	0.01	-0.06	0.09	0.27
ANPUB_POST	-0.04	-0.11	-0.21	-0.16	0.18	-0.18	-0.09	0.06
A_Choices	-0.15	0.51**	0.32	0.43*	0.10	0.22	0.57**	-0.18
BMI	0.14	0.26	0.12	-0.06	0.12	0.37*	0.20	1

EB: Exploited Balloons; ANPUB: Average Number of Pumps on Unexploded Balloons; T: total; U+: Positive Urgency;
EB: Exploited Balloons; ANPUB: Average Number of Pumps on Unexploded Balloons; T: total; U+: Positive Urgency;
U-: Negative Urgency; SS: Sensation Seeking; LPrem: lack of premeditation; LPers: lack of perseverance; A_Choices: appetizing choices; BMI: Body Mass Index

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

Table 5. Pearson correlations between variables in normal weight group are displayed.

n=27 Excess weight	Hunger_ Change	UPPSP_ T	UPPSP_ U+	UPPSP_ U-	UPPSP_ SS	UPPSP_ LPrem	UPPSP_ LPers	BMI
Hunger_change	1	0.14	-0.11	-0.05	0.49**	0.07	-0.11	-0.30
EB_Change	0.46*	0.03	-0.16	0.02	0.16	0.03	-0.18	0.06
ANPUB_Change	0.14	-0.19	0.14	0.21	-0.17	0.06	-0.17	-0.14
EB_PRE	0.32	0.07	0.08	0.26	0.38	0.15	0.42*	-0.01
EB_POST	0.60**	0.07	-0.07	0.21	0.41*	0.15	0.17	0.04
ANPUB_PRE	0.43*	0.26	-0.01	0.03	0.38	0.15	0.33	-0.01
ANPUB_POST	0.48**	0.02	0.08	0.26	0.27	0.16	0.14	-0.15
A_Choices	0.24	0.57**	0.20	-0.17	0.23	0.36	0.20	0.22
BMI	-0.30	0.12	0.22	0.08	0.01	0.17	0.39*	1

EB: Exploited Balloons; ANPUB: Average Number of Pumps on Unexploded Balloons; T: total; U+: Positive Urgency; U-: Negative Urgency; SS: Sensation Seeking; LPrem: lack of premeditation; LPers: lack of perseverance; A_Choices: appetizing choices; BMI: Body Mass Index

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

4. Discussion

Results showed that after the food-choice task adolescents with excess weight displayed increased values in the two risk-taking measures of the BART than adolescents with normal weight. Adolescents with excess weight also showed a greater increase in hunger levels (VAS scores) after exposure to the food-choice task. Furthermore, excess weight adolescents showed greater scores in Positive Urgency and Sensation Seeking (UPPS-P), as well as an increased number of appetizing selections in the food-choice task, compared to normal weight adolescents. Finally, significant associations were found between the change in hunger feelings, risk-taking and impulsivity measures.

Food-visualization effects on risk-taking

Our findings suggest that adolescents with excess weight have enhanced reactivity to food cues, since the food-choice task led to an increase in risk-taking in these individuals. Yeomans and Brace (2015) [32] showed similar results in a study comparing restrained *versus* overeating-susceptible healthy women selected according to their scores in on the disinhibition and restraint scales of the Three Factor Eating

Questionnaire (TFEQ) [33]. They found that exposure to food cues led to a greater risk propensity (measured with the BART) in women susceptible to overeating in comparison with restrained women. However, they found group differences in BART measures both before and after food cue-exposure, while we only observed differences after the food-choice task. The pre-task discrepancy may be due to differences in the studies samples, as they selected their sample based on uncontrolled eating (TFEQ), while we selected ours based on BMI.

To our knowledge, this is the first study to analyse the influence of food cues visualization on risk-taking in adolescents with excess weight. The fact that excess weight adolescents increase risky decision-making after food exposure may be relevant to our understanding of the role of food cues in the development of unhealthy eating behaviours in modern societies. Motivational mechanisms could be involved in food cue-enhanced risky decision-making. In general, it is known that positive mood states induce increased risk-taking [34], which in turn promotes further gratification-seeking behaviour to maintain a positive mood. For example, undergraduate college students are more likely to drink on days of celebration than during the week [35], and individuals may also engage in risky drinking to enhance a pre-existing positive mood [36]. This hypothesis is in line with our results of greater positive urgency (reward seeking under a positive mood) in excess weight adolescents. In line with this result, Fernández-Serrano y cols. (2011) [37], using the Iowa gambling task (IGT) in polysubstance users, found that drug-users (who showed a risky pattern of decision-making under normal conditions) decreased their risk-taking in a negative affective context (visualization of negative images while performing the IGT) to a level similar to that observed in controls, while they increased their risky decisions on the IGT during a positive affective context evoked by drug cue visualization.

Food-visualization effects on hunger levels and its associations with risk-taking

The food-choice task led to a greater increase in hunger feelings in excess weight group. Food cues could be associated with greater reward value in adolescents with excess weight than in normal weight adolescents. Evidence points to greater neural reactivity in the reward system in obese *versus* normal weight individuals during high-calorie food visualization [38]. Therefore, appetizing food cues may evoke an approach response to reward, leading to greater hunger feelings and enhanced impulsive risk-taking behaviours [39]. In fact, in our study, a greater number of appetizing choices in the food-choice task were found in excess *versus* normal weight adolescents. Therefore, this purported greater underlying reactivity to appetizing food cues in obese individuals may mediate the observed impulsive behaviour after food visualization.

Furthermore, we found a positive association between risk-taking (greater number of exploded balloons and average number of pumps on unexploded balloons) and the change in hunger levels in the whole sample and in the excess weight group particularly, but not in the normal weight group. Besides, the change in hunger levels was also positively associated with the average number of pumps of unexploded balloons after the food-choice task in adolescents with excess weight. Therefore, food visualization and the consequent increase in hunger lead to enhanced risk-taking in excess weight adolescents, what may cause alterations in impulses control and hinder the intake control. Furthermore, subjective hunger may predispose an individual to believe that his/her body is in a state of homeostatic imbalance that must be restored through the intake of food. This may increase the predisposition to overeat in current society, given the ubiquitousness of full of fatty/sweet food cues. Therefore, these results suggest that greater hunger feelings may predispose to enhanced risk-taking in

excess weight adolescents, which can lead to greater seeking of the reward consumption, in this case appetizing foods high in fats and / or sugars.

Impulsivity measures and its associations with hunger levels and appetizing choices

Excess weight adolescents showed greater scores in Positive Urgency and Sensation Seeking than normal weight adolescents. Available evidence concerning impulsivity traits in obese adolescents is scarce. In the two studies available on adolescents with excess weight, no groups differences in impulsivity were found [7, 40]. As a possible explanation for these differences *versus* the current study, the mean age of the excess weight participants in these previous studies was 14.19±1.38 and 14.22±1.4 years, lower than that in our study (15.28±1.82 years). The mean age of our study is characterized by greater freedom and less control by parents, so it is more likely that adolescents around this age develop behaviours such as searching for new experiences or immediate rewards. For example, significant relationships between sensation seeking and adolescent alcohol use, cigarette smoking and marijuana use have been reported, with older adolescents being more likely to engage in these types of risky behaviours [41]. Conversely, Nazarboland and Fath (2015) [42] found greater Sensation Seeking in highly obese adolescents (BMI>35) than in normal weight adolescents.

Sensation Seeking was positively associated with the change in hunger levels in excess weight participants. Furthermore, this variable mediated the difference in hunger levels in this group between the pre- and post- food-choice task evaluations. This suggests that the impulsivity trait may not only be associated with eating preferences, but also with changes in subjective feelings of hunger, which could stimulate overeating and the intake of high-calorie foods, leading to obesity.

Regarding to this, Sensation Seeking has long been associated with elevated drug intake in humans (43). Therefore, the influence of Sensation Seeking on a greater increase in hunger feelings in excess weight adolescents may support the hypothesis of a greater reactivity to food signals (i.e., increased seeking for rewards and positive reinforcement) in these participants.

A preference for appetizing food in the food-choice task was associated with impulsivity measures in our whole sample. Specifically, Sensation Seeking and Positive Urgency (both related to greater reward sensitivity), which may indicate a mediational role of impulsivity in determining food preferences. These results corroborate previous evidence. Davis y cols. (2007) [44] found in women ranging from normal weight to obese that reward sensitivity was positively linked to overeating and high sugar-fat food preferences. Nederkoorn y cols. (2010) [45] found that participants with greater impulsivity gained more weight during a 1-year period. It has been proposed that impulsivity may accelerate the acquisition of Pavlovian conditioning to appetitive cues [46]. All of this evidence suggests that exposure to appetitive food cues, via interaction with impulsivity traits, may play an important role in the development of unhealthy eating behaviours. In modern societies, given the high availability of, and frequent exposure to, high calorie foods, individuals with high reward sensitivity are predisposed to consumption beyond their caloric needs. The enhanced preference for fat-sweet foods is explained by their greater reinforcing value, especially in individuals with excess weight [47].

As the incentive salience of appetizing food cues increases, seeking out and consuming this type of food becomes an important goal, exceeding feeding homeostatic regulation [48]. This represents a risky behaviour, since consuming foods high in fat and/or sugar is associated with weight gain in children and adolescents and, therefore, increased risk

of obesity [49]. Macchi, MacKew and Davis (2017) [50] assessed eating habits and risk-taking (BART) in adolescents and found that choices on the BART were riskier in adolescents who made unhealthier food choices. These findings are congruent with studies observing that adolescents with higher risk-taking on the BART consistently engaged in greater risk-taking activities outside of the laboratory, such as smoking, drinking, gambling or substance abuse [51-53].

Limitations

Regarding limitations of the study, there are a number of issues that need to be addressed in future studies, like differentiating among obese, overweight and normal weight participants, the inclusion of objective eating behaviour measures (in the home and/or the lab), and the fulfilment of a more exhaustive decision-making evaluation. Furthermore, future studies should evaluate the longitudinal influence of risk-taking on weight gain. Finally, the lack of a control group not exposed to the food-choice task manipulation makes it difficult to discern whether the changes in hunger feelings and decision-making are due to the visualization of food, the mere passage of time or the repeated administration of the test. Future studies will be necessary to address this limitation by including an appropriate control group.

Conclusions

In summary, the results showed that excess weight adolescents increased their risky decision-making after food-choice task exposure, where this was associated with an increase in hunger levels. Furthermore, adolescents with excess weight displayed greater scores in impulsivity measures, which were positively associated with the number of appetizing choices in the food-choice task. Excess weight in adolescence is a risk factor for the development of future health problems and obesity. In current western societies, given the high availability of, and exposure to, high-calorie foods, decision-

making has become a crucial factor in maintaining healthy eating habits. Since risk-taking is more prevalent in adolescence, it may be important to empower adolescents to make healthy decisions to prevent future obesity. Impulse control and decision-making should be an important target to prevent risky eating behaviour in adolescents.

5. References

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Capítulo 9. Increased food choice-evoked brain activation in adolescents with excess weight: relationship with subjective craving

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1. Introduction

The prevalence of adolescent overweight and obesity has steeply increased over the last two decades, reaching epidemic levels (1). In most cases, overweight and obesity are the result of food choices characterized by high calorie intake. When these choices are consolidated at an early age, obesity is more severe and associated with worse long-term consequences (2).

Although food consumption is an essential human behaviour, factors that regulate dietary choices are complex and poorly understood. Food intake is influenced by a variety of factors besides homeostatic regulation, like sensory cues (e.g., taste, smell, texture and appearance), availability, motivational and affective states, pleasure seeking, etc. All of these aspects influence what, and how much, humans eat even when they are satiated. These factors are associated with specific patterns of regional cerebral blood flow (rCBF), particularly within brain regions commonly implicated in motivation, emotion, memory, and behavioural control (3).

Previous studies have demonstrated that brain activation in response to food pictures is a useful measure to examine both sensitivity to food cues and vulnerability to the development or maintenance of overweight (4, 5). High-fat foods evoked activation in brain regions associated with reward value processing (e.g. dorsal/ventral striatum, orbitofrontal cortex [OFC]), as well as with the representation of internal body states such as hunger (insula) (6, 7).

Comparisons of rCBF between obese and normal-weight individuals have shown differential responses to food cues associated with weight status (6, 8, 9). Obese individuals show greater activation to food cues in comparison to normal-weight participants in multiple brain regions, including reward system-related ones, like the

prefrontal cortex (PFC), OFC, anterior cingulate cortex (ACC), insula, amygdala, and striatum during hunger states (10); the PFC, caudate, hippocampus, and temporal lobe immediately after eating (8); and the striatum, insula, hippocampus, and parietal lobe during neutral appetitive states (neither hungry or satiated) (6). In addition, differential activation to food types (high- and low-calorie) has also been examined in relation to weight. The majority of reported results of direct comparisons between normal-weight and obese/overweight groups indicate greater activation in response to high-calorie food cues in similar brain regions among overweight/obese individuals (6, 8, 10).

Another way to study brain activation during eating behaviour is by using food choice paradigms. Food decisions concern what, when, and how much to eat. Food choices can lead to overconsumption, when more energy is consumed than expended. The brain mechanisms underpinning food choices have been examined in neuroimaging studies. Several neural processes are involved in feeding behaviour. Firstly, the visual system is very important to guide food selection. Inputs from the visual system elicit a specific pattern of brain activation related to preparation for food ingestion, which evokes the desire to eat, as well as cognitive processes such as memory retrieval and hedonic evaluation of the specific food (11, 12). Secondly, visual food cues activate the reward neural circuitry (e.g., PFC, OFC, amygdala, dorsal and ventral striatum, hypothalamus, and insula) (10). Moreover, high-calorie food cues specifically elicit a greater response in these regions relative to low-calorie food images (13, 14).

Recent theoretical models highlight that decision-making skills are a key factor in controlling caloric intake in modern environments, since these are characterized by open access to food and strong media-driven appeals to eat high-calorie food (15). Decision-making skills are particularly pertinent in the case of adolescents, in whom transitions in brain development appear to be geared towards maximizing reward at the expense of

risk (16). Neuroimaging studies have confirmed that adolescents have hypersensitive striatal responses to reward prediction (17, 18) and high activation of brain areas implicated in the promotion of risk-taking (OFC) during decision-making (19).

However, the neural correlates of food choices in adolescents have been less well-studied. This matter is particularly important, as the probability that an obese adolescent develops into an obese adult is much higher than that of a normal-weight adolescent (20). Moreover, once people have become overweight or obese, it is quite difficult for them to regress to a stable healthy weight. The important increase in the prevalence of obesity in children and adolescents, the complications of overweight / obesity for health and the greater tendency to continue being overweight or obese in adulthood make prevention of obesity the alternative of choice and the optimal strategy to stop the spread of the obesity epidemic.

In this study, we used functional magnetic resonance imaging (fMRI) to assess brain regions associated with food choices between appetizing (i.e., high sugar, high fat) and plain food in adolescents with excess weight (i.e., overweight and obese) versus normal weight. We also aimed to evaluate the association between choice-evoked brain activation and subjective self-reported food craving. We hypothesized that excess weight participants, in comparison with the normal weight ones, would show greater neural responsiveness in the corticolimbic reward system during food choices between appetizing and plain foods (i.e., OFC, ACC, insula, ventral striatum and amygdala). We also hypothesized that this choice-evoked activation in these areas would correlate with food craving in the excess-weight group.

2. Methods

Participants

Seventy-three adolescents (age range: 14-19 years) participated in the study. They were classified into two groups, excess weight [n=38] (27 adolescents with obesity and 11 adolescents with overweight) or normal weight [n=39], according to their age- and sex-adjusted body mass index (BMI) percentile, following the International Obesity Task Force (IOFT) criteria (21). There were no significant differences in age or sex between groups. Demographic and body composition data are summarized in Table 1.

The recruitment of participants was carried out throughout the province of Granada (Andalusia, Spain) in hospitals and high schools, as well as via press and radio advertisements. The inclusion criteria were defined as follows: (i) aged between 14 and 19 years; (ii) BMI percentiles falling within the intervals categorized as overweight or obesity (≥85: Excess weight group), or normal weight (5 to 84: Normal weight group); (iii) absence of any history or current evidence of neurological mental disorders as assessed via interviews with participants and their parents; (iv) absence of any history or current evidence of eating disorders (e.g., binge eating, bulimia nervosa, anorexia nervosa) assessed with the Eating Disorders Inventory-2 (EDI-2) and (v) absence of any contraindication to undergo the fMRI session (i.e. metal prosthesis or claustrophobia). All participants had normal or corrected-to normal vision.

The study was approved by the Ethics Committee for Human Research of the Universidad de Granada. Both the participants and their parents signed an informed consent form.

Table 1

Socio-demographic characteristics, BMI and percentage of fat for each group.

	Excess weight (n=38) Mean (SD[b])	Normal weight (n=39) Mean (SD)	t[c]/chi square[d]	p-value
Age	16.47 (1.66)	16.58 (1.36)	-0.30[c]	0.768
Sex (%men/women	47.37/52.63	48.72/51.28	0.00[d]	0.991
BMI[a]	29.89 (3.72)	21.36 (2.07)	12.58[c]	< 0.001
Fat (%)	29.03 (10.28)	15.61 (7.39)	6.56[c]	< 0.001

[a:] Body Mass Index; [b]: Standard Deviation; [c]: value of Student's t; [d]: value of Chi-square $\chi 2$

Procedure

This study consisted of two sessions. In the first session, all participants were pre-exposed to foods in a catered tasting session conducted 1 week before scanner acquisition. The participants tasted all foods included later in the fMRI task in order to become familiar with the specific foods (and their corresponding flavours, textures and sizes) that were going to be used in the fMRI tasks. The purpose of the tasting was to establish a context closer to real life in the food choice task. Then, they had to rate the different foods on a 1- to 10-point self-report scale indexing how much they liked each meal.

In the second session, we conducted the fMRI task. When participants arrived at the lab, we used an automated scale (Tanita BC-420 GP Supplies Ltd., London) to measure their weight and body fat percentage. Body fat percentage was estimated via Bioelectrical Impedance Analysis. All of the sessions were carried out at the same time of day (4 p.m.), and always fMRI tasks were carried out between one and three hours after lunch. The teenagers finished their lessons in the high school about 2.30 p.m., after that they took lunch and at 4 p.m. they started the session. Given the study had a larger protocol that included more measures assessed before fMRI, participants usually started the fMRI tasks at about 5 p.m. Just before the fMRI session, before beginning the task

inside the scanner, and after finishing the fMRI session, participants rated their hunger from 0 to 100 points on a visual analogue scale in response to the question of "how hungry are you now?"

fMRI task

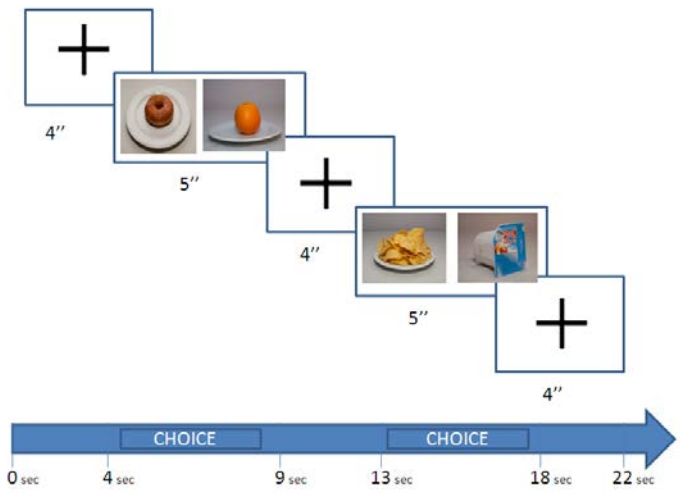
A food preference decision-making task was used. The food pictures used in the task were taken earlier in the tasting session. All pictures were shot ad hoc for the study using standardized presentation and lighting conditions. Therefore, all images were matched for visual properties and serving size (about a portion to all food images). Three types of food were utilized: appetizing (food with high levels of fats and sugars), plain (defined as natural food or low in fats and/or sugars) and functional (foods that are prepared not only for their nutritional characteristics but also to fulfil a specific function, such as improving health and reducing the risk of disease). Appetizing cues included, for instance, sausages, chocolate, cake, cheese and chips and plain cues included, for instance, fruits, yoghurt, cereals and salads. In each trial, pairs of these different types of food were presented to participants (appetizing vs. plain, appetizing vs. functional and plain vs. functional). Participants were instructed to choose between these two options taking into account their own preference for one or the other meal. The question presented was: "If you had to eat one of these foods, which would you choose?" Each trial began with a fixation cross, which appeared for 4 seconds. Then, images of the two options appeared for 5 seconds (one on the left side of the screen and the other one on the right side). The order of presentation of the images was counterbalanced among the participants. Then, the fixation cross was presented again (Fig 1). There were a total of 36 choice trials with 12 choices for each decision type. Participants were instructed to press a button in order to choose the food that they preferred. Stimuli were presented through magnetic resonance-compatible liquid crystal

display goggles (Resonance Technology Inc., Northridge, CA, USA), and responses were recorded with the Evoke Response Pad System (Resonance Technology Inc.). Participants were instructed to press the button with their thumb if they preferred the food on the left side, or the button with their forefinger for food on the right side. According to the objectives of this study, we focused only on the choice between appetizing food and plain food. The primary behavioral measure was the number of selections of appetizing and plain foods.

After the fMRI session, participants assessed their "craving" for each food presented earlier in the scanner on a 9-points scale (1, they did not desire the meal; 9, desired the meal excessively). Valence and arousal for each meal were also assessed via Self-Assessment Manikin (SAM) (22). The stimuli were presented using a computer task programmed using e-Prime software, in which each stimulus was presented on the screen for 5 seconds. The difference of score between subjective ratings of craving in response to appetizing versus plain food (referred to as “Appetising vs. Plain Craving”) was calculated.

Figure 1

Schematic representation of the fMRI task through depiction of the sequence of one experimental trial



Imaging data acquisition and processing

A 3.0 T clinical MRI scanner (Intera Achieva; Philips Medical Systems, Eindhoven, The Netherlands), equipped with an eight-channel phased-array head coil, was used to obtain a T2*-weighted echo-planar imaging sequence with the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 35 ms, field of view (FOV) = 230 × 230 mm, 96 × 96 matrix, flip angle = 90°, 21 4 mm axial slices, 1 mm gap, 162 scans. A sagittal three-dimensional T1-weighted turbo-gradient-echo sequence (3DTFE) (160 slices, TR = 8.3 ms, TE = 3.8 ms, flip angle = 8°, FOV = 240 × 240, 1 mm^3 voxels) was also obtained in the same experimental session to discard gross anatomical abnormalities.

Functional images were analyzed using Statistical Parametric Mapping (SPM8) software (Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, UK), running on MATLAB R2009 (MathWorks, Natick, MA). Prior to preprocessing, all images were visually inspected for artifacts. Preprocessing included reslicing to the first image of the time series, slice timing correction, normalization (using affine and smooth nonlinear transformations) to an EPI template in Montreal Neurological Institute (MNI) space, and spatial smoothing by convolution with a 3D Gaussian kernel (full width at half maximum = 8 mm). No participant was excluded due to excessive motion, defined as a degree of movement above 3 mm or 3 degrees in either direction.

Data analysis

Group comparisons of sociodemographic, task, and self-reported variables were performed with independent-sample t-tests (two-tailed).

For the neuroimaging analysis, the conditions of interest were modelled from the time at which the food choice was presented to the time at which participants responded.

Baseline was modelled as the time that the fixation cross was on the screen. Task regressors were convolved with the SPM8 canonical hemodynamic response function. The key contrast of interest was "appetizing vs. plain > baseline", defined in first-level (single subject) and between-group analyses.

One-sample t-tests were conducted to assess intra-group activations (healthy weight and excess weight) in the contrasts of interest. Between-group comparisons were conducted using two-sample t-tests. The statistical threshold used for all fMRI analyses, (i.e: intra- and between-group analyses) was $p< 0.05$ false discovery rate (FDR) whole-brain corrected, with a minimum cluster size extent (KE) of 10 contiguous voxels.

Finally, in order to examine the association between choice-evoked brain activation and subjective food craving, the peak beta eigenvalues from each cluster of significant brain differences between groups were extracted for each participant and correlated with the "Appetising vs. Plain Craving" variable.

3. Results

No significant group differences in preferences for appetizing, plain or functional food, or in any of the self-reported measures, were obtained (see Table 2).

Table 2

Means (±SD) of food choices and self-reported measures (tasting, valence, arousal, craving and hunger).

	Excess weight (n=37) Mean (SD)	Normal- weight (n=36) Mean (SD)	p-value
Appetizing food			
Food Tasting	7.59 (1.09)	7.74 (1.15)	0.571
Valence	6.45 (1.09)	6.58 (1.19)	0.633
Arousal	5.32 (1.63)	5.48 (1.45)	0.657
Craving	5.61 (1.29)	5.75 (1.49)	0.679
Plain food			
Food Tasting[a]	7.43 (1.06)	7.28 (1.08)	0.552
Valence	6.22 (1.04)	6.2 (1.19)	0.956
Arousal	5.15 (1.43)	5.23 (1.22)	0.801
Craving	5.35 (1.13)	5.26 (1.38)	0.745
Number of Appetizing choices	14.62 (4.51)	15.64 (4.71)	0.349
Number of Plain choices	14.11 (3.85)	14.28 (3.21)	0.839
%Appetizing-Plain choices	53.24 (20.57)	54.81 (18.97)	0.734
Appetizing vs. Plain	0.26 (0.93)	0.49 (0.73)	0.238
Craving			
Hunger1[b]	20.69 (21.2)	19.84 (18.9)	0.861
Hunger2[c]	18.42 (21.06)	27.7 (24.56)	0.102
Hunger3[d]	36.68 (27.67)	46.43 (28.15)	0.156

Brain activation during appetizing vs. plain food choices compared to baseline (fixation cross)

Both groups show extensive activation in brain regions in response to the appetizing versus plain food choices, including areas of the frontal cortex (dorsolateral prefrontal cortex [dlPFC], dorsomedial prefrontal cortex [dmPFC] and ventrolateral prefrontal cortex [vlPFC]), occipital cortex (visual cortex), and subcortical regions (thalamus, caudate, striatum, insula and amygdala) (see table S1).

Differences in patterns of brain activation between excess- and normal-weight participants

The excess weight group, compared to the normal weight group, displayed increased activation in the dlPFC (bilaterally), superior temporal cortex (bilaterally), hippocampus, medial temporal cortex, putamen, superior frontal cortex, thalamus (bilaterally), globus pallidus, inferior temporal cortex, OFC, ventrolateral prefrontal cortex, dorsal ACC, insula and dorsal caudate during food choice processing (see Table 3). The normal-weight group had no additional activation versus the excess weight group in any brain area (see Figure 2).

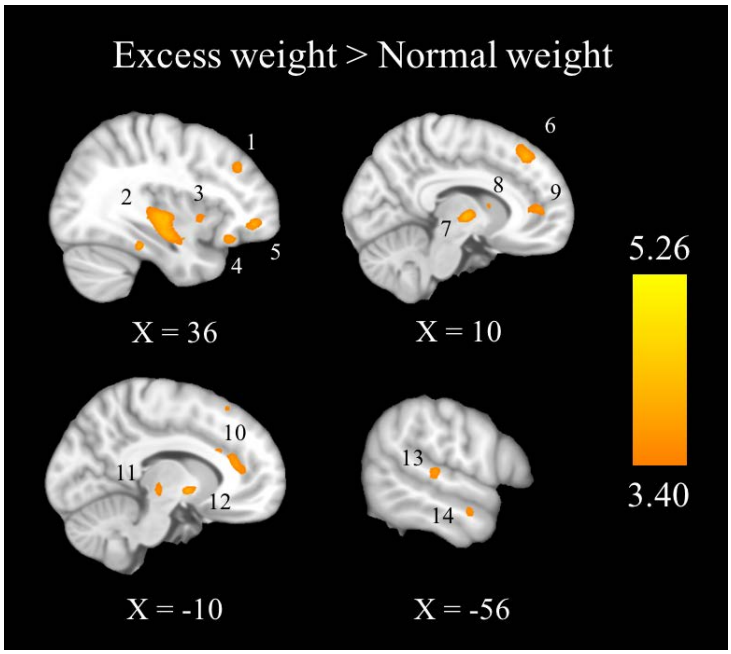
Table 3

Brain regions that show greater activation in "appetizing versus plain choices > baseline" in excess weight group than in the normal weight group.

Region	Side	MNI coordinates			Ke[a]	t-value
		X	Y	Z		
dlPFC[b]	Right	32	34	36	133	4.12
	Left	-34	44	10	199	5.26
STCx[f]	Right	60	-20	2	364[c]	4.58
	Left	-52	-30	6	131	4.19
Hippocampus	Right	42	-16	-18	945[d]	4.46
MTC[g]	Right	46	-36	2	364[c]	4.37
Putamen	Right	34	-16	0	945[d]	4.34
SFCx[h]	Right	10	36	48	241	4.32
Thalamus	Right	10	-8	2	945[d]	4.3
	Left	-6	-20	0	152	3.82
GlobusPallidus	Left	-12	-2	-4	51	4.22
ITC[i]	Left	-60	-4	-18	93	4.15
OFC[j]	Right	38	48	-6	182[e]	4.13
vlPFC[k]	Right	30	30	-20	182[e]	3.96
Rostral ACC[l]	Right	6	48	4	91	3.88
ACC	Left	-10	36	16	96	3.82
Insula	Right	40	6	-4	48	3.7
DorsalCaudate	Right	12	10	8	23	3.74

Figure 2

Between-group differences during "appetizing vs. plain > baseline" contrast.



1: dlPFC: dorsolateral prefrontal cortex; 2: Putamen; 3: Insula; 4: vlPFC: ventrolateral prefrontal cortex; 5: OFC: orbitofrontal cortex; 6: SFC: superior frontal cortex; 7: Thalamus; 8: Dorsal Caudate; 9: Rostral ACC: rostral anterior cingulate cortex; 10: ACC: anterior cingulate cortex; 11: Thalamus; 12: Globus Pallidus; 13: STC: superior temporal cortex; 14 ITC: inferior temporal cortex.

Association between brain activation and subjective food craving

In the excess-weight group "Appetising vs. Plain Craving" correlated with appetizing versus plain food choice-evoked activation in the dorsolateral and ventrolateral prefrontal cortices, ACC, insula, superior/medial/inferior temporal cortices, dorsal caudate, putamen and thalamus while in the normal-weight group only insula was correlated with "Appetising vs. Plain Craving" (see Table 4). We performed an FDR adjustment for multiple comparisons and the regions that remained significant were the right dlPFC, dorsal caudate and superior temporal cortex only in the excess weight group.

Table 4

Correlations between craving scores (Appetizing vs. Plain Craving) and "appetizing versus plain choices > baseline" brain activation as a function of group. Only areas with significant correlations are displayed.

					Excess weight		Normal weight		Fisher
	Side	MNI coordinates			p-value	r	p-value	r	p
		x	y	Z					
dlPFC[b]	Left	-34	44	10	**0.04**	**0.35**	0.43	-0.136	0.017
	Right	32	34	36	**0.001**[a]	**0.53**	0.819	-0.04	0.004
TSC[c]	Right	60	-20	2	**0.003**[a]	**0.49**	0.84	0.035	0.017
TMC[d]	Right	46	-36	2	**0.04**	**0.34**	0.221	0.209	0.274
Putamen	Right	34	-16	0	**0.01**	**0.43**	0.385	0.149	0.097
TIC[e]	Left	-60	-4	-18	**0.03**	**0.38**	0.628	0.083	0.092
vlPFC[f]	Right	30	30	-20	**0.03**	**0.38**	0.388	0.148	0.145
Thalamus	Left	-6	-20	0	**0.02**	**0.4**	0.892	-0.023	0.03
ACC[g]	Left	-10	36	16	**0.009**	**0.44**	0.381	0.15	0.089
Insula	Right	40	6	-4	**0.03**	**0.38**	**0.049**	**0.33**	**0.405**
DorsalCaudate	Right	12	10	8	**0.004**[a]	**0.48**	0.738	0.058	0.025

[a]: These results survived FDR correction for multiple comparison;[b]: Dorsolateral Prefrontal Cortex; [c]: Temporal Superior Cortex; [d]: Temporal Medial Cortex; [e]: Temporal Inferior Cortex; [f]: Ventrolateral Prefrontal Cortex; [g]: Anterior Cingulate Cortex

4. Discussion

We found that adolescents with excess weight, compared to those with normal weight, have higher brain activation in frontal, striatal, insular and mid-temporal regions during choices between appetizing and plain food cues and, furthermore, this activation correlated with subjective measures of craving. Neural responses in these regions during food cue exposure in the obese participants were consistent with previous studies (6, 10, 23-25), but there is a lack of studies focused on food choices in adolescents with excess weight; adolescence is an extremely important life stage, since it can be considered as the step prior to the development of obesity in adulthood. Furthermore, the context in which food choices are made is a novel field of research within this population. Decision making with respect to food choices may be considered the basis of healthy eating habits.

During brain activation in our food choice task, we observed significantly increased neural responses in the excess-weight group in the dlPFC and vlPFC, which are implicated in cognitive control (26, 27). Research in the decision-making and self-control literatures points to the particular importance of these regions (28-30). In fact, it is possible that the greater activation in these areas relates to inhibitory processes in response to the general belief that high-calorie foods are unhealthy and should be avoided. This increased activation in the inhibitory system may be a reaction to greater reward processing, as evoked by the high calorie stimulus (10). This fact may indicate that in overweight adolescents confronted with appetizing-healthy choices, stronger top–down control by the dlPFC on subcortical regions is necessary to produce the appropriate behavioural control (31). In fact, our findings are consistent with Davids y cols (2010) (25) who also found increased activation of dlPFC to food cues in obese children and also explained this fact as a greater inhibitory control effort. Therefore, the greater inhibitory control may be the cause of the lack of group differences in behavioural measures. Furthermore, adolescents with excess weight may present a bias regarding their eating choices, since adolescents are more susceptible to social desirability because of the importance given to their peer's opinions. Social desirability has been described as a tendency to overestimate desirable traits and behaviors and underestimate undesirable ones, when using self-reported measures (32). Among children and adolescents, socially desirable responding is considered part of normal development (33). In this case, adolescent with excess weight may think that to choose appetizing food cues is frowned upon due to his body image and, therefore, they end up choosing the healthy option. Klesges y cols, (2004) (34) reported that participants underestimates of sweetened beverage preferences and lower ratings of weight concerns and dieting behaviors were related to social desirability.

Another part of the PFC showing increased activation in our excess weight group was the OFC. This area plays an important role in food-related neural circuitry and responds preferentially to high-calorie food cues (6, 10). The OFC integrates multiple sources of information regarding reward outcomes to derive a value signal. According to Grabenhorst and Rolls (2011) (35), the reward value is 'passed' onward from the OFC to higher cognitive regions such as vlPFC, dlPFC and ACC. Regarding our results, increased activation in the OFC in excess weight adolescents may indicate greater processing of high-calorie food cues in terms of reward. The ACC, which was also more activated by the appetizing versus healthy food choice in our study, is thought to integrate this reward value with information about planned or anticipated actions and associated costs (35).

On the other hand, the excess weight group showed increased activation in the insula. The insula and OFC are interconnected as the primary and secondary gustatory cortex. A large number of studies found that insula is involved in craving (36), with specific reactivity to visual food cues, as well as anticipation and consumption of foods in obese individuals (37), and environmental drug cues in drug abusers (38). These results are in accordance with previous studies (13, 14, 39) showing the involvement of temporo-insulo-opercular and orbitofrontal networks in food processing. Furthermore, Yoku, Ng and Stice (2011) (40) found that youth who showed elevated reward circuitry responsivity, specifically in OFC, during appetizing food cue exposure were at increased risk for weight gain.

Finally, we found greater activation in the dorsal striatum (caudate and putamen) in the appetizing versus plain food choice. This area is a part of the habit learning system, which has previously been linked to lowered dopamine D2 receptor availability in obese (41) and drug-addicted individuals (42-46).

The reward deficiency theory has been advanced to clarify how a baseline hypo functioning dopamine system may lead to compulsive intake of substances of abuse, as individuals attempt to self-medicate via direct manipulation of neurotransmitter levels (47). This model has also been proposed for individuals with excess weight, similarly self-medicating by overconsumption of high-fat/high-sugar foods (47-49). Dopamine is involved in encoding the pleasure associated with food intake. Highly appetizing foods and drugs of abuse directly affect the mesolimbic system, with consumption of each type of substance increasing dopamine levels (50, 51). The incentive-sensitization model of obesity posits that repeated pairings of reward from food intake and cues that predict impending food intake result in a hyper-responsivity of dopamine-based reward circuitry to food cues, contributing to craving and overeating (52). Therefore, in our study, food choice-induced anticipation of palatable food can elevate activity in the fronto-limbic circuitry, thought to correspond to striatal dopamine release (50, 53).

In general, our findings showed greater brain reactivity to food cues in adolescents with excess weight. Neural food cue reactivity as indexed by fMRI has been shown to be prospectively associated with food choice (54, 55), snack consumption (5), future weight gain in adolescent girls (40), and women (56), weight status in women (57) and outcome in a weight-loss program (58). Therefore, our findings may be extremely relevant to appropriate decision-making of food consumption. In fact, there are already preliminary results that show that regional brain activity elicited by food cues of high incentive salience is reduced during 'motivational neurofeedback', in which participants receive real-time feedback of this activity through changes in the cue's visible size, also showing a significant reduction of hunger after successful downregulation (59).

As a second result, we found a positive relation between the variable "Appetizing vs. Plain Craving" and brain activation in the food choice task only in the excess weight

group. This result might imply that the desire and subjective value that excess weight adolescents give to food cues is important, and related to the cognitive processing that they engage in when choosing between appetizing and plain food cues. This outcome is consistent with the results of Jastreboff y cols. (2013) (60), who found that in obese but not lean individuals, food craving correlated positively with neural activity in corticolimbic-striatal brain regions during presentation of favourite foods. It seems that it is not only people with obesity show greater food reactivity and subsequent craving, but also overweight (without reaching obesity levels). On the other hand, in a food choice processing, normal weight adolescents seem to give less importance to the subjective value of food cues given their lack of associations between craving and brain processing. However, there are no differences in behavioral craving between groups. This fact may be due to the social desirability as we have commented previously. In a recent systematic review, Boswell and Kober, (2016) (61) demonstrated a robust prospective and predictive relationship between measures of food cue reactivity, including the conscious experience of craving and subsequent food-related outcomes. Overall, their results suggested that food cue reactivity and craving explained a substantial amount (7–26%) of the variance in food-related outcomes. The abundance of food and food cues in the modern 'toxic food environment' may function as conditioned stimuli that serve as triggers for increased food consumption and can lead to weight gain on a population level (62-64).

All of our results support the "food addiction model". Brain areas showing food-craving-related activation in this study have been reported to be activated in drug craving studies. The relationship between the dorsal striatal network and food craving was significant in the overweight group in this study, in accordance with the notion of an addictive dimension of obesity. Moreover, we found a positive relationship between

dlPFC activation and craving, which may suggest that participants who require more inhibitory control during the appetizing-plain food choice show more craving for this high-calorie food (and hence there is a need for greater control). In summary, a bunch of regions seems to be involved in the experience of affect or emotion, memory, higher-level processing of chemosensory stimuli, and the establishment of incentive salience. However, there are several limits to these similarities between drug and food addiction that should be addressed in upcoming investigations.

The main conclusion of this study is that adolescents with excess weight have increased activation in several regions involved in reward and emotional salience when they are faced to choose between appetizing versus plain food. The results also suggest that adolescents with excess weight ascribe greater importance to the incentive value of appetizing food, since subjective craving correlated with the brain regions activated during food choices, although no differences in behavioral craving were found between groups. The difference between groups in relation to craving was only observed at brain level.

The findings of the present study have treatment implications. Interventions for obese adolescents should not solely focus on prominent or physical symptoms, but should also target basic cognitive control functions and processes related to the emotion-processing system, such as altered reward-related decision making, to address specific impairments in patients with excess weight. Our results also show the importance of interventions focused on strategies to enhance inhibitory control in this population, in order to improve the outcomes of obesity treatments. The ability to resist temptations and craving in response to high-calorie food is extremely important to prevent unhealthy eating behaviors. Cue reactivity and craving to food cues may be directly relate to real-life behavior, given that their effect on subsequent food-related outcomes is comparable

with real food exposure. Therefore, to promote a reduction in exposure to food cues in the environment of adolescents with excess weight could be an important target for obesity prevention policies.

Furthermore, more research into the neural correlates of food choice may provide better insight into the effects of age, sex, and weight on food-related decision-making processes, and provide targets for healthy eating interventions. Since an overweight child or adolescent has a high probability of developing into an overweight adult, prevention of overconsumption of unhealthy foods and formation of healthy eating habits in children is crucial in order to reverse the prognosis.

This study had some limitations, such as the type of contrast that we used (appetizing and plain food cues vs. baseline), since some of the activations are not specifically related to decision making. However, this limitation was partially overcome due to the fact that significant correlations were found with the craving measure. On the other hand, although we observed clear and extensive differences between our obese and control samples, because we used a cross-sectional experimental design, it was not possible to determine whether the observed effects represent the causes or consequences of obesity. Moreover, it would be interesting if the functional implications of the current results could be addressed in longitudinal studies. Furthermore, research is needed to compare the results obtained between participants in fasted and satiated states. Finally, the effects of the menstrual cycle should be taken into account in future studies, since a number of studies have reported that brain activation and decision making processes are modulated by the hormonal stage of the menstrual cycle during exposure to food cues (65, 66).

Conclusion

In summary, this neuroimaging study strongly supports the hypothesis of behavioural studies whereby overeating in obese individuals is triggered by exaggerated reactivity to stimuli associated with high-calorie foods. It might be expected, for example, that an exaggerated activation of the reward system in response to high-incentive food cues would predict weight gain, especially in subjects at risk for obesity. Conversely, the magnitude of activation in response to high-incentive food cues might discriminate between those who were subsequently successful or unsuccessful in losing weight and/or maintaining weight loss. It would be of interest to determine whether the responsiveness of a hyperactive reward system could be moderated in response to successful anti-obesity therapy, and whether such neuroadaptation would lead or follow the weight loss.

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IV. DISCUSIÓN, CONCLUSIONES Y PERSPECTIVAS FUTURAS

Capítulo 10

Discusión

Uno de los principales retos del siglo XXI a nivel mundial es el abordaje del problema de la obesidad. Por tanto, el estudio de los factores que contribuyen a la creciente prevalencia de este problema es, sin duda, uno de los principales desafíos científicos actuales. Diversos modelos científicos han postulado que el conocimiento de los mecanismos de procesamiento cerebral, así como los procesos cognitivos asociados, puede aportar información muy útil a la hora de explicar la ocurrencia y el mantenimiento de la obesidad (Rangel, 2013). La revisión de la literatura realizada al inicio de nuestra investigación nos permitió comprobar la existencia de alteraciones cognitivas en la población con obesidad, paralelismos con la adicción a drogas, así como peculiaridades sociales y biológicas propias de la etapa de la adolescencia. Observamos, sin embargo, que existía un escaso número de estudios sobre aquellos factores que podrían predisponer y estar asociados con el exceso de peso en la adolescencia. Partiendo de esta premisa, los objetivos de esta tesis pueden resumirse principalmente en tres. El primero estaba dirigido a analizar el efecto del estrés social, muy frecuente en adolescentes con exceso de peso, sobre el rendimiento cognitivo y la actividad fisiológica asociada a este. El segundo objetivo estaba dirigido a examinar la influencia de la visualización de una tarea de elección alimenticia sobre la toma de decisiones de riesgo en adolescentes con exceso de peso, así como analizar la asociación con variables de impulsividad, el nivel de hambre subjetivo, el tipo de elecciones alimenticias y el IMC. Por último, el tercer objetivo estaba dirigido al análisis de la activación cerebral ante una tarea de elección alimenticia en adolescentes con exceso de peso, así como a estudiar la asociación de esta activación cerebral con el *craving* subjetivo reportado por los alimentos mostrados en la tarea.

Los resultados de nuestros estudios avalaron las hipótesis propuestas: encontramos diferencias entre los adolescentes con exceso de peso y los adolescentes con normopeso, en la mayoría de los procesos estudiados.

En relación con nuestro primer objetivo, este se dividió en dos objetivos específicos que se corresponden con los dos primeros estudios que conforma esta tesis. El primer estudio consistió en analizar la influencia del estrés social en procesos de atención y toma de decisiones, mientras que el segundo investigó dicha influencia en el rendimiento ejecutivo. Los resultados obtenidos en el primer estudio mostraron que el estrés social produce un efecto perjudicial en el rendimiento atencional en los adolescentes con exceso de peso, y que, a su vez, este decremento en el rendimiento estaba asociado a un mayor aumento del cortisol en este grupo. En cuanto al segundo estudio, los resultados también revelaron un efecto perjudicial del estrés social en el rendimiento ejecutivo en el grupo de adolescentes con exceso de peso. Además, este déficit estuvo asociado con una mayor reactividad autonómica en el grupo de exceso de peso.

En relación con nuestro segundo objetivo, los resultados de nuestro tercer estudio mostraron que los adolescentes con exceso de peso presentaban mayor cantidad de elecciones de alimentos apetitosos (altos en grasas y/o azúcares) así como mayor puntuación en algunas variables de impulsividad como urgencia positiva y búsqueda de sensaciones. Así mismo, los resultados también manifestaron que la visualización de imágenes de alimentos impactaba en una mayor toma de riesgos en el grupo de exceso de peso, así como una asociación positiva entre la toma de riesgos y la cantidad de alimentos apetitosos elegidos y las variables de impulsividad.

Por último, en relación a nuestro tercer objetivo, los resultados de nuestro cuarto estudio mostraron que los adolescentes con exceso de peso tenían mayor activación cerebral en áreas relacionadas con la recompensa al visualizar una tarea de elección alimenticia. Así mismo, esta activación estaba asociada positivamente, en el grupo de exceso de peso, con el *craving* que mostraban los participantes por los alimentos presentados en la tarea.

En conjunto, estos resultados tienen una serie de implicaciones tanto teóricas como clínicas que abordaremos a continuación.

1. Implicaciones teóricas

En relación a las implicaciones del primer estudio, los resultados mostraron que los adolescentes con sobrepeso y obesidad presentan mayor reactividad en respuesta a estresores sociales, reflejado en un mayor aumento de cortisol, lo que impactaba selectivamente en sus capacidades atencionales. Por otro lado, nuestros resultados son particularmente relevantes en cuanto a las asociaciones significativas entre la reactividad del cortisol y los comportamientos relacionados con la ganancia de peso (Lu y cols., 2014, van Strien, Roelofs & de Weerth, 2013), y la emergente evidencia que sugiere que niveles altos de estrés puede predecir longitudinalmente la progresión de la obesidad (Kubzansky y cols., 2014). Así mismo, el efecto perjudicial del estrés social en la capacidad atencional también tiene importantes implicaciones ya que otros estudios han comprobado que las alteraciones individuales en las latencias de respuesta se asocian longitudinalmente con aumentos en el IMC (Frazier-Wood y cols., 2014). Esta noción es consistente con nuestro hallazgo de correlaciones significativas entre una menor mejoría del rendimiento atencional tras el estresor social en el grupo de exceso de peso y patrones de alimentación maladaptativos más elevados, como la alimentación externa, que refleja un sesgo atencional hacia las señales relacionadas con los alimentos.

Además, tanto el estrés social como el déficit en las habilidades atencionales están significativamente asociados con un peor funcionamiento social y rendimiento académico (Rouach y cols., 2007).

En cuanto a las implicaciones de nuestro segundo estudio, los resultados mostraron, al igual que en el primer estudio, que los adolescentes con exceso de peso mostraban mayor reactividad ante el estrés social, y en concreto ante las evaluaciones negativas, reflejado en una mayor actividad autonómica y mayores niveles de estrés subjetivo. Además, esta situación de estrés social provocaba un efecto perjudicial en el rendimiento ejecutivo del grupo con exceso de peso, el cual estaba asociado con la mayor actividad autonómica durante la fase de evaluación social negativa. Las implicaciones son similares a las del estudio anterior, pero hemos de añadir que las funciones ejecutivas son tremendamente importantes en lo que se refiere a control del comportamiento, por tanto, creemos que estos resultados son cruciales para entender por qué el impacto del estrés social puede derivar en un peor control de impulsos y, por tanto, en una posible sobreingesta. De hecho, los déficits ejecutivos han sido asociados con comportamientos relacionados con la obesidad en la infancia (mayor ingesta, alimentación desinhibida, y reducción del ejercicio físico). Por tanto, estos déficits pueden conllevar que los adolescentes con exceso de peso persistan en sus hábitos alimenticios no saludables. En conjunto, observamos que el estrés social produce un efecto perjudicial en el rendimiento cognitivo en los adolescentes con exceso de peso.

En cuanto a las implicaciones teóricas del tercer estudio, los resultados sugieren que los adolescentes con exceso de peso tienen mayor reactividad a las señales alimenticias, ya que la tarea de elección alimenticia provoca un incremento tanto en la toma de riesgos como en los niveles de hambre en este grupo. Además, el grupo con exceso de peso presentó mayor nivel de impulsividad reflejado en mayores puntuaciones en las

variables de Urgencia Positiva y Búsqueda de Sensaciones, así como un mayor número de elecciones de alimentos apetitosos en la tarea de elección alimenticia. Asimismo, se encontraron en toda la muestra asociaciones positivas entre los cambios en los niveles de hambre y la toma de riesgos, así como asociaciones con las variables de impulsividad y el IMC. Hasta nuestro conocimiento, este es el primer estudio que analiza la influencia de la visualización de señales de comida en la toma de riesgos en adolescentes con exceso de peso. Además, el grupo de adolescentes con exceso de peso también mostraron mayor nivel de urgencia positiva, lo que indica una mayor tendencia a la búsqueda de refuerzos bajo estados de ánimo positivos. Estos resultados están en línea con los hallazgos de Fernández-Serrano y cols. (2011), los cuales mostraban que los poli-consumidores de sustancias incrementaban su toma de riesgos en la IGT en contextos afectivos positivos, como la visualización de señales de drogas. Así mismo, una mayor preferencia por los alimentos apetitosos en la tarea de elección alimenticia estuvo asociada positivamente con las medidas de Urgencia Positiva y Búsqueda de Sensaciones en nuestra muestra. Estos resultados corroboran la evidencia previa de que participantes con mayores niveles de impulsividad eran más propensos a la sobreingesta de alimentos altos en grasas y/o azúcares y por tanto a la ganancia de peso (Davis y cols., 2007; Nederkoorn, Houben, Hofmann, Roefs & Jansen, 2010). Toda esta evidencia sugiere que la exposición a señales de alimentos apetitosos en interacción con rasgos impulsivos, puede jugar un importante rol en el desarrollo y mantenimiento de hábitos alimenticios no saludables. En las sociedades occidentales modernas, dada la alta disponibilidad y la frecuente exposición a alimentos con alto contenido calórico, las personas con alta sensibilidad a la recompensa están predispuestas a la sobreingesta, ignorando sus necesidades calóricas. La mayor preferencia por los alimentos grasos y/o dulces se explica por su mayor valor reforzante, especialmente en personas con exceso

de peso. Esto representa un comportamiento de riesgo, ya que el consumo de este tipo de alimentos está asociado con el aumento de peso en niños y adolescentes y, por lo tanto, con un mayor riesgo de obesidad (Millar y cols., 2014). Por último, el mayor incremento del hambre en el grupo con exceso de peso y la asociación positiva entre la toma de riesgos y los niveles de hambre sugiere que el nivel subjetivo de hambre puede predisponer a un individuo a creer que su cuerpo está en un "falso" estado de desequilibrio homeostático que debe restaurarse mediante la ingesta de alimentos.

En cuanto a las implicaciones teóricas del cuarto estudio, los hallazgos aportados por los patrones de activación durante la neuroimagen indican que los adolescentes con exceso de peso presentan una mayor activación de áreas relacionadas con la recompensa (regiones frontales, estriatales, insulares y medio-temporales) ante una tarea de elección entre imágenes alimenticias, lo que podría indicar una mayor sensibilidad ante las señales de comida. La mayoría de los estudios que han encontrado mayor activación cerebral en el circuito de la recompensa durante la exposición a señales de comida se han realizado en participantes con obesidad (Scharmüller, Übel, Ebner & Schienle, 2012; Connolly y cols., 2013; Rothemund y cols., 2007; Stoeckel y cols., 2008). Por tanto, nuestros resultados son innovadores ya que muestran un procesamiento cerebral incrementado en personas con IMCs asociados a sobrepeso, sin tener que llegar a presentar un IMC asociado a obesidad. Además, la mayoría de los estudios también se centran en adultos, por lo que hemos abordado de manera más profunda los factores asociados al exceso de peso en un período tan crítico como es la adolescencia.

Los adolescentes con exceso de peso también mostraron mayor activación en el dlPFC. Nuestra explicación de este hecho está basada en otros estudios que sugieren que existe un mayor esfuerzo para redirigir su preferencia alimenticia por lo que utilizan un mayor control inhibitorio, así como por el concepto de deseabilidad social (Davids y cols.,

2010; Klesges y cols., 2004). Esto explicaría que no haya diferencias conductuales en las elecciones alimenticias entre los dos grupos. Por otro lado, la mayor activación en el OFC que muestran los adolescentes con exceso de peso está asociado, según los resultados de diferentes estudios, con un riesgo incremento de ganancia de peso (Yokum, Ng & Stice, 2011). En cuanto a la mayor a activación del estriado dorsal, este resultado está en línea con los modelos de la auto-medicación o "reward deficiency syndrome RDS" que proponen que existe un nivel basal más bajo de DA en el sistema mesolímbico en personas con obesidad, al igual que ocurre en personas adictas a sustancias, y que resulta en una falta de placer o refuerzo proveniente de actividades que normalmente si lo proporcionan (Volkow y cols, 1996; 1997; Volkow & Wise, 2005; Heinz y cols., 2004; Martínez y cols., 2004). Siguiendo este modelo, los alimentos altamente apetitosos y las drogas de abuso afectan directamente al sistema mesolímbico, y el consumo de dichas sustancias aumentaría los niveles de DA cerebral conllevando así un aumento del placer (Small, Jones-Gotman & Dagher, 2003; Rada, Avena & Hoebel, 2005). Por lo tanto, en nuestro estudio, la anticipación inducida por la elección de alimentos apetitosos puede elevar la actividad en el circuito fronto-límbico, que se corresponde con la liberación de DA en el sistema estriatal y así generar un efecto reforzante. Así mismo, la mayor reactividad cerebral ante señales alimenticias ha sido asociada de forma positiva con el consumo de snacks entre horas y el incremento de peso y, de forma negativa con los resultados en un programa de pérdida de peso (Lawrence, Hinton, Parkinson & Lawrence, 2012; Yokum y cols., 2011; Demos, Heatherton & Kelley, 2012; Murdaugh, Cox, Cook & Weller, 2012). Por tanto, nuestros resultados sugieren que el procesamiento cerebral ante señales alimenticias es un factor extremadamente importante a tener en cuenta en cuanto al control del comportamiento alimenticio se refiere.

Un segundo resultado que encontramos en nuestro cuarto estudio fue la asociación positiva entre la activación cerebral ante la tarea de elección alimenticia y el craving informado por los participantes con exceso de peso. Este resultado podría implicar que el deseo y el valor subjetivo que los adolescentes con exceso de peso otorgan a las señales alimenticias son muy importantes, ya que están estrechamente asociados con el procesamiento cerebral que realizan ante una tarea de elección alimenticia. Además, la evidencia sugiere que la reactividad ante las señales de alimentos junto con el craving explica una cantidad importante de la varianza en los resultados relacionados con las intervenciones en exceso de peso (Boswell & Kober, 2016), mostrándose como fuertes predictores en este sentido. Como conclusión, todos estos resultados apoyan el modelo de "adicción a la comida" basado en los existentes paralelismos entre los mecanismos neurobiológicos subyacentes en la adicción a sustancias y la obesidad (Volkow y cols., 2013a; 2013b), aunque es necesaria mucha más investigación en este ámbito.

2. Implicaciones clínicas

Las implicaciones clínicas de nuestros resultados son múltiples y se pueden agrupar en dos: (i) la contribución que realizan a la comprensión de la importancia de la intervención en el exceso de peso en la adolescencia, y (ii) las aportaciones que realizan en cuanto a la mejora del conocimiento de la influencia de las señales alimenticias en multitud de procesos y, por tanto, su necesaria inclusión en los programas de intervención.

En cuanto a la primera contribución, derivada de nuestro primer y segundo estudio, podemos concluir que la presencia y alta frecuencia del estrés social en adolescentes con exceso de peso puede tener influencias perjudiciales en el rendimiento cognitivo en esta población y esto puede conllevar al aumento de la ingesta a través de múltiples

factores (alimentación emocional, falta de control de impulsos, persistencia en los patrones de alimentación, etc). Por lo tanto, intervenciones basadas en estrategias de manejo del estrés, así como herramientas alternativas para afrontar las situaciones de "alimentación emocional" que eviten el uso de la sobreingesta como estrategia de afrontamiento, son extremadamente importantes de cara a evitar las posibles consecuencias negativas que el estrés social crónico pueda estar causando en el origen o mantenimiento del exceso de peso. A su vez, el entrenamiento en habilidades sociales y de afrontamiento del estrés en situaciones sociales puede mejorar el desempeño social en esta población y, por ende, mejorar su autoestima y bienestar, así como su rendimiento académico que como hemos visto anteriormente también se puede ver afectado negativamente. En segundo lugar, derivado del tercer estudio podemos afirmar que en los adolescentes con exceso de peso se produce un aumento en sus niveles de hambre y toma de riesgos después de la visualización de señales de alimentos y, dado que en la adolescencia la toma de riesgos e impulsividad es mucho mayor, las intervenciones centradas en este aspecto son fundamentales. Por ejemplo, se podrían llevar a cabo intervenciones centradas en el entrenamiento de la capacidad para demorar la recompensa y para aumentar el tiempo que se dedica a decidir, llevando a cabo un razonamiento más profundo sobre las ventajas e inconvenientes tanto a corto como a largo plazo de cada elección. De esta manera, los adolescentes podrían llegar a adquirir las habilidades necesarias para cambiar sus hábitos alimenticios basados en alimentos que ofrecen una recompensa inmediata por aquellas opciones saludables que ofrecen una recompensa beneficiosa para su salud más a largo plazo. En general, son necesarios tratamientos que fomenten la mejora del control del comportamiento, a través de intervenciones basadas en la mejora de las funciones ejecutivas, ya que creemos que esto impactará en sus comportamientos alimenticios. Por último lugar, en relación a los

resultados del cuarto estudio, y teniendo en cuenta las singularidades psicobiológicas que presenta la etapa de la adolescencia (mayor importancia del sistema hedónico de recompensa a expensas de las áreas relacionadas con el control ejecutivo), observamos que en los adolescentes con exceso de peso presentan mayor activación de áreas relacionadas con la recompensa aunque también presentan mayor activación en áreas implicadas en el control del comportamiento como es el dlPFC. Este último resultado implica que los adolescentes con exceso de peso intentan inhibir la conducta no saludable a nivel cerebral pero que no es suficiente para suprimir finalmente el comportamiento. Estudios recientes apuestan por la técnica de estimulación transcraneal con corriente directa (tDCS) como una herramienta eficaz en el tratamiento de la obesidad. Concretamente, la mayoría de los estudios se centran en la estimulación del dlPFC como estrategia para reducir el craving por la comida y la consecuente ingesta (Uher y cols., 2005; Barth y cols., 2011; Forcano, Mata, de la Torre & Verdejo-García, 2018). Como conclusión, los resultados de esta tesis evidencian el papel crítico de la adolescencia en la aparición y desarrollo del exceso de peso y la obesidad.

El segundo grupo de implicaciones clínicas de esta tesis doctoral se focalizaría sobre la influencia de las señales alimenticias en los comportamientos relacionados con la ingesta de alimentos. A través del tercer y cuarto estudio, hemos comprobado la reactividad que presentan los adolescentes con exceso de peso a este tipo de señales y su asociación con variables como el hambre, toma de riesgos o *craving.* Por tanto, nuestros resultados indican que es necesario implementar intervenciones dirigidas a la prevención de comportamientos alimenticios no saludables. Por ejemplo, hemos observado que la reactividad y el *craving* a las señales alimenticias pueden estar directamente relacionados con el comportamiento en la vida real, ya que sus efectos en los resultados posteriores relacionados con el comportamiento alimenticio son

comparables con la exposición a comida real. Por tanto, consideramos que promover una reducción en la exposición a señales alimenticias en el contexto de los adolescentes con exceso de peso debe ser un objetivo cardinal en las políticas de prevención de la obesidad. De hecho, ya hay resultados preliminares que muestran que la actividad cerebral provocada por señales de alimentos de alto valor hedónico se reduce durante el "neurofeedback motivacional", en el que los participantes reciben retroalimentación de esta actividad en tiempo real a través de cambios en el tamaño de las señales alimenticias, mostrando una reducción significativa del hambre después de una auto-regulación inhibitoria del comportamiento (Ihssen, Sokunbi, Lawrence, Lawrence, & Linden, 2017). Por tanto, nuestros resultados indican que sería adecuado implementar intervenciones centradas en la auto-regulación inhibitoria del comportamiento del individuo con el fin de poder adquirir estrategias que permitan resistir a la tentación tras la visualización de alimentos apetitosos. Así mismo, sería conveniente el desarrollo de políticas basadas en la reducción de mensajes que promueven el consumo de alimentos altos en grasas y/o azúcares, así como las señales alimenticias derivadas de esta publicidad. Esta medida ayudaría a la prevención del desarrollo de la obesidad, y específicamente, el desarrollo de la obesidad en la adolescencia, una etapa más vulnerable debido a todos los factores comentados anteriormente.

En resumen, nuestros datos apoyan los resultados de estudios previos (Batterink, Yokum y Stice, 2010; Nederkoorn y cols, 2006, 2010; Lowe y Fisher, 1983) que apuntan que la obesidad podría estar relacionada con una mayor reactividad emocional y un pobre control inhibitorio, y añadimos nuevos resultados como la influencia perjudicial del estrés social, la mayor toma de riesgos tras la exposición a señales de alimentos y la asociación entre la activación cerebral y el *craving* en el grupo de adolescentes con exceso de peso. En conclusión, consideramos de vital importancia la

inclusión de intervenciones centradas en la capacitación de los adolescentes con exceso de peso para el afrontamiento exitoso del estrés, mejora de habilidades ejecutivas y de control del comportamiento que impacten en una menor toma de riesgos y un comportamiento alimenticio saludable, estrategias para resistir la tentación ante señales y alimentos altamente calóricos y, por último, y de forma general, el intento de reducción de las señales alimenticias de alto contenido calórico en nuestro actual ambiente.

3. Fortalezas y limitaciones

Uno de los principales puntos fuertes de nuestros estudios es la metodología empleada para la selección de la muestra. Variables sociodemográficas como el sexo, la edad y los años de educación se encuentran igualados entre grupos. Además, diversos trastornos metabólicos (p.ej. diabetes, hipertensión, obesidad mórbida) y psicopatológicos (p.ej. depresión, y trastornos alimenticios como bulimia o trastorno por atracón) fueron causa de exclusión de nuestras investigaciones, garantizando que las diferencias encontradas entre grupos se debieran exclusivamente a los factores analizados y no a otros trastornos comórbidos. Por último, la gran variedad de técnicas utilizadas (fMRI, registro psicofisiológico, evaluación neuropsicológica, medidas de autoinforme, etc.) enriquece los resultados obtenidos.

Estos resultados podrían estar limitados por algunos condicionantes. Por un lado, la naturaleza correlacional de nuestros estudios no permite inferir causalidad y, por tanto, otras explicaciones alternativas pueden ser posibles. Otra posible limitación es la utilización de varias muestras por lo que hay que tener precaución a la hora de trasladar las conclusiones obtenidas entre los estudios.

Capítulo 11

Conclusiones

A partir de los resultados obtenidos en los distintos estudios de esta tesis, se derivan las siguientes conclusiones:

1. El estrés social produce un deterioro en pruebas que miden la capacidad atencional en los adolescentes con exceso de peso. Este deterioro está asociado a una mayor reactividad psicofisiológica, medida a través de cortisol salival.
2. La evaluación social negativa produce un deterioro ejecutivo (incluyendo medidas de memoria de trabajo, inhibición y flexibilidad) en los adolescentes con exceso de peso. Este deterioro está asociado una mayor reactividad psicofisiológica, medida a través de la tasa cardíaca y la conductancia electrodermal.
3. Los adolescentes con exceso de peso presentan mayor reactividad a las señales alimenticias ya que tras su visualización aumenta en mayor medida sus niveles de hambre y presentan una mayor toma de riesgos. Además, los adolescentes con exceso de peso presentan mayores puntuaciones en algunos rasgos de impulsividad, como la Urgencia Positiva y la Búsqueda de Sensaciones, los cuales están asociados con el aumento del hambre y la toma de riesgos en este grupo.
4. Los adolescentes con exceso de peso presentan una mayor activación en áreas cerebrales relacionadas con el circuito de la recompensa ante la visualización de una tarea alimenticia. Esta activación, en este grupo, se asocia positivamente con el *craving* por los alimentos mostrados en la tarea.

En general, nuestros resultados resultan innovadores puesto que contribuyen a señalar algunos de los factores que pueden estar influyendo en el exceso de peso, además de señalar la importancia de la intervención en la adolescencia debido a sus características diferenciales en múltiples aspectos: mayor estrés social, toma de riesgos e impulsividad,

además de las singularidades psicobiológicas propias de esta etapa. Todos estos factores hacen que la adolescencia sea un período crítico a la hora de desarrollar o mantener problemas relacionados con comportamientos compulsivos, y en particular, con la sobreingesta de alimentos. De estos resultados también se desprende la importancia de tener en cuenta las señales de alimentos altamente calóricos (imágenes, anuncios publicitarios, escaparates, etc.) como elemento disparador de la conducta alimenticia e incluirlo en los programas de intervención con el fin de promover estrategias para controlar la tentación derivada de la continua exposición a éstos. Además, dado que los niños y adolescentes con sobrepeso tienen una alta probabilidad de convertirse en adultos con sobrepeso, la prevención del consumo excesivo de alimentos no saludables y la formación de hábitos alimenticios saludables en estas etapas es crucial para revertir el pronóstico.

Capítulo 12

Perspectivas futuras

Las conclusiones derivadas de esta tesis nos permiten generar nuevas preguntas de investigación que creemos sería interesante explorar en estudios futuros. Entre ellas podríamos destacar:

1. Profundizar en el conocimiento de los efectos del estrés social en la conducta alimenticia de los adolescentes con exceso de peso a través de estudios longitudinales que permitan el establecimiento de relaciones causales entre ambos.
2. Evaluar a través de investigaciones más ecológicas si, efectivamente, la visualización de alimentos altos en grasas y/o azúcares conlleva una mayor ingesta de estos alimentos, y por tanto impacta en un mayor aumento de peso.
3. Estudiar más profundamente a través de fMRI los correlatos neurales de las elecciones con alimentos reales. Analizar la actividad cerebral durante todo el proceso, es decir antes de realizar la elección y cuando se consume el alimento y observar las diferencias entre un grupo de adolescentes con exceso de peso y uno con normopeso. Esta metodología permitiría que los resultados obtenidos fueran más fácilmente transferibles a la vida real.
4. Realizar intervenciones centradas en el *craving* que presentan los adolescentes con exceso de peso hacia alimentos altamente calóricos con el objetivo de controlar la tentación, y ver si las modificaciones en el valor hedónico que se le otorga a los alimentos tiene consecuencias en el procesamiento cerebral ante la visualización de éstos.
5. Realizar estudios utilizando la técnica tDCS para intentar reducir el craving a través de la estimulación repetida del dlPFC mejorando así las capacidades de autocontrol del individuo; y estudiar la viabilidad de incluir esta técnica en programas de tratamiento de la obesidad.

6. Analizar si a través de un programa de intervención centrado en el afrontamiento de estrés se producen resultados beneficiosos en los hábitos alimenticios a través de modificaciones en los comportamientos relacionados con la "alimentación emocional". Así la reducción del impacto el estrés social también influiría en la disminución de los efectos perjudiciales en sí que produce el estrés crónico en la cognición.
7. Analizar el efecto de los genes relacionados con la transmisión de la dopamina, en concreto DRD2-A1 y DRD4-7R, en el rendimiento ejecutivo de adolescentes con exceso de peso. Diferentes estudios han mostrado que padecer obesidad y tener el alelo DRD4-7R parecer conferir una debilidad en términos de rendimiento ejecutivo. Sin embargo, los estudios son escasos, con muestra insuficiente y no están centrados en los adolescentes con exceso de peso.

V. DOCTORADO INTERNACIONAL

1. Summary

The increase in the obesity prevalence has become, in recent decades, according to the World Health Organization, one of the main public health problems worldwide. Obesity is a complex condition in which many factors intervene. In ancient times, people regulated their intake according to their metabolic states of hunger and satiety, however, in today's western societies what and how much to eat has become a decision-making matter. Recent studies suggest that the change in current lifestyle, based on sedentary lifestyle and unhealthy eating habits, is responsible for the dramatic increase in the prevalence of obesity.

Excess weight and obesity have also increased exponentially in childhood and adolescence, critical stages in the development of the individual. Adolescence is a stage in which the individual is especially vulnerable due to its behavioral peculiarities. In this stage, behaviours aimed at the reward search and propensity to risk are frequent, as well as a decrease in executive control and the ability to regulate behavior effectively. In this regard, various studies confirm the existence of disturbances in executive functioning in overweight adolescents compared with adolescents with healthy weight. The executive functions allow a better regulation of the behavior, and specifically, of the eating behavior.

Furthermore, excess weight in adolescence not only causes negative consequences at the health level (type II diabetes, higher probability of developing obesity in adulthood and its harmful medical consequences, etc.) but it is also associated with a social stress increase due mainly to the frequent teasing referred to their body image that they receive from their peers and that can even lead to marginalization and social exclusion. Therefore, adolescents with excess weight suffer greater social

stress in their day to day. Numerous studies point to the detrimental effect of stress on cognitive performance. Also, stress may also alter eating patterns through various mechanisms.

As we have commented previously, the homeostatic mechanisms have gone to second place to explain the eating behavior, being the decision-making processes extremely important in this matter. Specifically, impulsive behavior can play an important role in obesity during childhood and adolescence. Different studies have shown that the cues visualization related to drug use produces an increase in impulsivity levels and induces a greater risk taking, increasing as a consequence the risk of consumption in individuals addicted to substances. Also, several studies show that people with excess weight have an attentional bias and greater reactivity towards food signals high in fats and / or sugars.

Moreover, in recent years, various studies underscore the superimposition of the neurobiological pathways involved in substance abuse and obesity resulting in the creation of the concept "food addiction". The drugs of abuse use the same neural mechanisms that modulate the motivation to consume food; therefore, there is a parallelism between the brain circuits involved in the loss of control and excessive food intake that characterizes obesity and compulsive drug use. The alteration of the dopamine brain circuits is central in these two pathologies. Specifically, the brain reward system is a central component to develop and monitor motivated behaviours. Therefore, knowledge of its functioning is vital to better understand the problem of obesity. During exposure to highly appetizing foods, reward circuit areas may promote greater dopamine release due to the great salience of the stimulus and thus lead to a greater predisposition to overeating. It also happens in studies with populations addicted to substances during exposure to drugs cues. In general, the

results of fMRI studies carried out so far point to an increased response in areas of the reward circuit, both in adults and in overweight adolescents, when processing food images, especially those with a high fat content and sugars.

Taking into consideration all previous, the objectives of this doctoral thesis were: 1) study the influence of social stress on neuropsychological performance in adolescents with excess weight and adolescents with normal weight, 2) analyse the influence of food cues visualization in a risk decision-making task and its relationship with impulsivity, in adolescents with excess weight compared to adolescents with normal weight, y 3) analyse brain processing during food choices and its relation to subjective craving, in excess weight adolescents and normal weight adolescents.

To address these objectives, 4 studies were carried out. The results obtained showed: 1) social stress is associated with worse attentional and executive performance in excess weight adolescents who also experience greater autonomic reactivity to this stress compared to adolescents with normal weight (study 1 and 2); 2) adolescents with excess weight make more risky decisions after exposure to food cues and have higher levels of impulsivity than adolescents with normal weight (study 3); and 3) there is greater activation of brain areas related to the reward circuit during the exposure to food-choice task in the group of excess weight adolescents and an association between activation in these areas and the craving reported by the participants towards the foods presented in the task was found (study 4).

These results could be very useful at a theoretical level, contributing to the advancement of knowledge of the factors that are predisposing to weight gain in

adolescence, as well as to clinical level, promoting new treatments that take into account neuropsychological and emotional variables that contribute to improve paediatric interventions aimed at reducing the excess weight problems.

2. Conclusions

From the results obtained in the different studies of this thesis, the following conclusions are derived:

1. Social stress produces deterioration in tasks that measure the attention capacity in adolescents with excess weight. This deterioration is associated with a greater psychophysiological reactivity, measured through salivary cortisol.
2. Negative social assessment produces executive impairment (including measures of working memory, inhibition and flexibility) in excess weight adolescents. This deterioration is associated with a greater psychophysiological reactivity, measured through heart rate and electrodermal response.
3. Adolescents with excess weight have a greater reactivity to food cues since after their visualization they increase their hunger levels and they present a greater risk taking. In addition, adolescents with excess weight present higher scores in some traits of impulsivity, such as Positive Urgency and Sensations Seeking, which are associated with increased hunger and risk taking in this group.
4. Adolescents with excess weight have greater activation in brain areas related to the reward circuit when they are exposed to a food task. This activation, in this group, is positively associated with craving for the foods shown in the task.

In general, our results are innovative since they help to point out some of the factors that may be influencing excess weight, as well as pointing out the importance of intervention in adolescence due to its differential characteristics in multiple aspects:

greater social stress, risk taking and impulsivity, in addition to the psychobiological peculiarities of this stage. All these factors make adolescence a critical period when it comes to developing or maintaining problems related to compulsive behaviors, and in particular, with overeating. These results also reveal the importance of taking into account the highly caloric foods cues (images, advertisements, shop windows, etc.) as a trigger element of eating behavior and include it in intervention programs in order to promote strategies for control the temptation derived from the continuous exposure to them. In addition, since children and adolescents with excess weight have a high probability of becoming overweight adults, the prevention of excessive consumption of unhealthy foods and the formation of healthy eating habits in these stages is crucial to reverse the prognosis.

3. Future perspectives

The conclusions derived from this thesis allow us to generate new research questions that we believe would be interesting to explore in future studies. Among them we could highlight:

1. Deepen the knowledge of the effects of social stress on the eating behavior of excess weight adolescents through longitudinal studies that allow the establishment of causal relationships between them.
2. Evaluate through more ecological research if, effectively, the visualization of foods high in fats and / or sugars leads to a greater intake of these foods, and therefore impacts on a greater weight gain.
3. Study more deeply through fMRI the neural correlates of elections with real foods. Analyse the brain activity during the whole process, that is before making the choice and when the food is consumed and observe the differences between

a group of adolescents with excess weight and one with normal weight. This methodology would allow the results obtained to be more easily transferable to real life.

4. Carry out interventions focused on craving presented by adolescents with excess weight towards high caloric foods in order to control the temptation, and see if the change in the hedonic value that is given to food has consequences in brain processing display of these.
5. Conduct studies using the tDCS technique to try to reduce craving through the repeated stimulation of the dlPFC, thus improving the self-control capabilities of the individual; and study the feasibility of including this technique in obesity treatment programs.
6. Analyse if through an intervention program focused on coping with stress, beneficial results are produced in eating habits through changes in behaviours related to "emotional eating". Thus, reducing the social stress impact would also influence the reduction of the detrimental effects that chronic stress produces on cognition.
7. Analyse the effect of genes related to the transmission of dopamine, specifically DRD2-A1 and DRD4-7R, on the executive performance of adolescents with excess weight. Different studies have shown that obesity and having the allele DRD4-7R seem to confer a weakness in terms of executive performance. However, studies are scarce, with insufficient sample and are not focused on adolescents with excess weight.

VI. **REFERENCIAS BIBLIOGRÁFICAS**

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VII. ANEXOS

ARTÍCULOS PUBLICADOS

Verdejo-Garcia, A., Moreno-Padilla, M., Garcia-Rios, M. C., Lopez-Torrecillas, F., Delgado-Rico, E., Schmidt-Rio-Valle, J., & Fernandez-Serrano, M. J. (2015). Social stress increases cortisol and hampers attention in adolescents with excess weight. PloS one, 10(4), e0123565. doi: 10.1371/journal.pone.0123565

Abstract

Objective: To experimentally examine if adolescents with excess weight are more sensitive to social stress and hence more sensitive to harmful effects of stress in cognition.

Design and Methods: We conducted an experimental study in 84 adolescents aged 12 to 18 years old classified in two groups based on age adjusted Body Mass Index percentile: Normal weight (n=42) and Excess weight (n=42). Both groups were exposed to social stress as induced by the virtual reality version of the Trier Social Stress Task -- participants were requested to give a public speech about positive and negative aspects of their personalities in front of a virtual audience. The outcome measures were salivary cortisol levels and performance in cognitive tests before and after the social stressor. Cognitive tests included the CANTAB Rapid Visual Processing Test (measuring attention response latency and discriminability) and the Iowa Gambling Task (measuring decision-making).

Results: Adolescents with excess weight compared to healthy weight controls displayed increased cortisol response and less improvement of attentional performance after the social stressor. Decision-making performance decreased after the social stressor in both groups.

Conclusion: Adolescents who are overweight or obese have increased sensitivity to social stress, which detrimentally impacts attentional skills.

Padilla, M. M., Fernández-Serrano, M. J., Verdejo García, A., & Reyes del Paso, G. A. (2018). Negative Social Evaluation Impairs Executive Functions in Adolescents With Excess Weight: Associations With Autonomic Responses. Annals of Behavioral Medicine. doi: 10.1093/abm/kay051

Abstract

Background: Adolescents with excess weight suffer social stress more frequently than their peers with normal weight.

Purpose: To examine the impact of social stress, specifically negative social evaluation, on executive functions in adolescents with excess weight. We also examined associations between subjective stress, autonomic reactivity, and executive functioning.

Methods: Sixty adolescents (aged 13–18 years) classified into excess weight or normal weight groups participated. We assessed executive functioning (working memory, inhibition, and shifting) and subjective stress levels before and after the Trier Social Stress Task (TSST). The TSST was divided into two phases according to the feedback of the audience: positive and negative social evaluation. Heart rate and skin conductance were recorded.

Results: Adolescents with excess weight showed poorer executive functioning after exposure to TSST compared with adolescents with normal weight. Subjective stress and autonomic reactivity were also greater in adolescents with excess weight than adolescents with normal weight. Negative social evaluation was associated with worse executive functioning and increased autonomic reactivity in adolescents with excess weight.

Conclusions: The findings suggest that adolescents with excess weight are more sensitive to social stress triggered by negative evaluations. Social stress elicited deterioration of executive functioning in adolescents with excess weight. Evoked increases in subjective stress and autonomic responses predicted decreased executive function. Deficits in executive skills could reduce cognitive control abilities and lead to overeating in adolescents with excess weight. Strategies to cope with social stress to prevent executive deficits could be useful to prevent future obesity in this population.

Moreno-Padilla, M., Fernández-Serrano, M. J., & del Paso, G. A. R. (2018). Risky decision-making after exposure to a food-choice task in excess weight adolescents: Relationships with reward-related impulsivity and hunger. PloS one, 13(8), e0202994. doi: 10.1371/journal.pone.0202994

Abstract

Objective: To assess the effects of exposure to a food-choice task (appetizing versus healthy food) on risky decision-making by excess versus normal weight adolescents. We also analyzed the influence of food visualization on hunger levels, as well as group differences in food choices and impulsivity.

Methods: Fifty-six adolescents (aged 13–18 years) classified as excess (n = 27) or normal (n = 29) weight participated in the study. Risky-decision-making was assessed through the Balloon Analogue Risk Task, which was administered before and after a food-choice task. We also evaluated impulsivity traits through the UPPS-P Scale, and subjective hunger levels with a visual analogue scale.

Results: Adolescents with excess weight showed enhanced risky decision-making after the food-choice task compared to normal weight adolescents, as well as increased hunger levels. Furthermore, excess weight adolescents made more appetizing choices, and showed greater scores for Positive Urgency and Sensation Seeking. Reward-related impulsivity measures were positively associated with the number of appetizing choices in the food-choice task. Several associations were found between impulsivity measures, hunger levels and risk-taking variables.

Conclusions: Excess weight adolescents increased their risky-decision-making after food exposure and this augmentation was associated with the increase in hunger levels. Increased hunger levels and risk-taking after food exposure could lead to overeating. Alterations in decision-making caused by food signals may be a long-term risk factor for the development of obesity in adulthood. In modern societies, with the high availability and continuous exposure to food cues, decision-making may be a crucial factor in maintain healthy eating habits in adolescents.

Moreno-Padilla, M., Verdejo-Román, J., Fernández-Serrano, M. J., del Paso, G. A. R., & Verdejo-García, A. (2018). Increased food choice-evoked brain activation in adolescents with excess weight: Relationship with subjective craving and behavior. Appetite, 131, 7-13. doi: 10.1016/j.appet.2018.08.031

Abstract

Objective: We used functional magnetic resonance imaging (fMRI) to assess brain regions associated with food choices between appetizing (i.e., high sugar, high fat) and plain food in adolescents with excess weight and those with normal weight. The associations between choice-evoked brain activation and subjective food craving and behavioral food choices were also evaluated.

Methods: Seventy-three adolescents (aged 14-19 years), classified into excess weight (n=38) or normal weight (n=39) groups, participated in the study. We used a foodchoice fMRI task, between appetizing and plain food, to analyse brain activation differences between groups. Afterwards, participants assessed their "craving" for each food presented in the scanner.

Results: Adolescents with excess weight showed higher brain activation in frontal, striatal, insular and mid-temporal regions during choices between appetizing and standard food cues. This pattern of activations correlated with behavioral food choices and subjective measures of craving.

Conclusions: Our findings suggest that adolescents with excess weight have greater food choice-related brain reactivity in reward-related regions involved in motivational and emotional responses to food. Increased activation in these regions is generally associated with craving, and increased dorsolateral prefrontal cortex is specifically associated with appetizing food choices among adolescents with excess weight, which may suggest greater conflict in these decisions. These overweight- and craving associated patterns of brain activation may be relevant to decision-making about food consumption.