# ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS

**Núria Voltas Moreso**

**Dipòsit Legal: T 956-2014**

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TESI DOCTORAL

dirigida per la Dra. Josefa Canals

Departament de Psicologia

UNIVERSITAT ROVIRA I VIRGILI

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Josefa Canals Sans, catedràtica del Departament de Psicologia de la Universitat Rovira i Virgili,

CERTIFICO:

Que el present treball, titulat "Estudi epidemiològic prospectiu de la simptomatologia emocional a l'inici de l'adolescència: seguiment en tres períodes evolutius", que presenta Núria Voltas Moreso per a l'obtenció del títol de Doctora, ha estat realitzat sota la meva direcció al Departament de Psicologia d'aquesta universitat.

Tarragona, 3 de març de 2014

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**Als meus pares**

**Als meus quatre avis**

**Al meu germà**

**A l'Eduard**

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## Agraïments

He pensat moltes vegades en aquest moment. És el moment de donar les gràcies a totes les persones que he sentit tan i tan properes durant aquest procés o que simplement formen part de la meva vida d'una manera especial.

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Núria

# ÍNDEX

UNIVERSITAT ROVIRA I VIRGILI
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# 1. Presentació

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# 1. Presentació

La present tesi doctoral sorgeix a partir d'un projecte finançat a través del *Fondo de Investigaciones Sanitarias* (PI07/0839) del *Instituto de Salud Carlos III* que porta per títol: "*Epidemiología de los trastornos depresivos y ansiosos en población escolar: perspectiva actual después de dos décadas de estudio"*, del qual la investigadora principal n'és la Dra. Josefa Canals i en què hem participat diversos investigadors.

En un primer moment es va portar a terme un estudi transversal en doble fase. La primera fase va consistir en la detecció de possibles símptomes d'ansietat, obsessius-compulsius i de depressió, en una mostra representativa d'escolars de centres de la ciutat de Reus. Després d'aquesta fase de detecció, es va procedir a la selecció d'una mostra de riscos (a partir dels subjectes que havien obtingut puntuacions de risc en algun dels qüestionaris de cribratge administrats a la primera fase), i una mostra de controls (subjectes que no havien obtingut puntuacions de risc en cap dels qüestionaris). Durant la segona fase, portada a terme amb els subjectes controls i riscos, es van obtenir diagnòstics de diferents trastorns psicopatològics, entre d'altres dades. Als dos anys següents, es va realitzar una tercera fase de seguiment dels 562 subjectes (riscos més controls) que havien participat a la segona fase. L'inici d'aquesta tercera fase va coincidir amb la meva arribada al grup de recerca, i me'n vaig responsabilitzar juntament amb els altres companys. L'objectiu principal era avaluar novament als subjectes un cop passats dos cursos acadèmics i veure com havien evolucionat, també tenint en compte que els subjectes ara es trobarien a l'inici d'una època tant marcada pels canvis, com és l'adolescència. A banda d'avaluar l'estat psicològic dels subjectes i d'altres variables com el rendiment acadèmic o la qualitat de les seves relacions socials, durant aquesta tercera fase també es van recollir dades antropomètriques i dades genètiques amb l'objectiu d'investigar polimorfismes genètics associats als

problemes emocionals i antropomètrics. Es va obtenir l'ADN dels subjectes a partir d'una mostra de saliva. Un cop finalitzada aquesta tercera fase en què lamentablement hi va haver una baixa participació, disposàvem d'una àmplia mostra de dades psicopatològiques, sociodemogràfiques, antropomètriques i genètiques, que ens permetrien analitzar la trajectòria dels trastorns emocionals des de la infància i fins a l'inici de l'adolescència. Aquestes dades també ens permetrien avaluar factors de risc i factors relacionats amb aquests símptomes, així com conseqüències de la seva presència per a la vida dels subjectes, i així poder realitzar una contribució a l'augment i a la millora del coneixement útil per a la realització d'una intervenció primerenca i eficaç i inclús útil per a la prevenció, que serviria per evitar un augment de la taxa de prevalença d'aquests trastorns en un futur.

# 2.Introducció

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# 2. Introducció

## 2.1. L'epidemiologia en psicopatologia infantil i juvenil

L'epidemiologia es defineix com la ciència que té l'objectiu d'avaluar la distribució, freqüència i factors relacionats o determinants d'una malaltia, o en el cas de l'epidemiologia en psicopatologia, d'un determinat trastorn psicopatològic en un determinat grup de persones (Merikangas i cols., 2009; Verhulst, 1995).

A nivell històric, es considera que els estudis epidemiològics en psicopatologia s'agrupen en tres generacions. La primera consisteix en estudis que es van centrar en l'anàlisi de la informació sociodemogràfica i clínica, recollida a través d'historials mèdics de pacients institucionalitzats i centrant-se molt en els factors causals de tipus biològic i hereditari. La segona generació d'estudis (posterior a la segona Guerra Mundial) es va caracteritzar per l'ús de les entrevistes administrades individualment, però els instruments només permetien ubicar al subjecte dins d'un continu amb els extrems: estar sa o patir una malaltia mental. Per últim, la tercera generació d'estudis s'inicia a finals dels anys setanta, coincidint amb un període en el qual els sistemes de classificació són més vàlids i ja existeixen instruments de mesura que permeten detectar la presència de trastorns mentals específics. Aquesta última generació d'estudis són els que marquen clarament l'inici de l'epidemiologia psiquiàtrica moderna, per tant, l'inici de l'epidemiologia tal i com la coneixem en l'actualitat. Per a que es produís aquest avenç, va ser de determinant importància la publicació del *Research Diagnostic Criteria (RDC)* (Spitzer i cols., 1978) i del *Diagnostic and Statistical Manual of Mental Disorders-III* (DSM-III) (American Psychiatric Association, 1980) com a criteris estardaritzats que van possibilitar el desenvolupament d'entrevistes diagnòstiques estructurades. També va ser un fet clau la utilització de noves estratègies de mostreig, la qual cosa va comportar una millora pel que fa a les mostres estudiades. En aquesta tercera etapa s'hi observen

dos enfocaments, per una banda els estudis realitzats als Estats Units, on es va optar per una metodologia basada en entrevistes diagnòstiques altament estructurades, creades a partir de criteris DSM. D'altra banda hi havia la corrent Europea, on es va optar més per l'ús de les entrevistes semiestructurades basades en criteris tant de l'APA (DSM) com de la OMS (ICD) i que necessitaven la intervenció d'un professional més qualificat. En aquest context, l'aparició de la primera entrevista diagnòstica estructurada, la *Diagnostic Interview Schedule* (DIS) (Robins i cols., 1981) va possibilitar que uns anys després aparegués el primer gran estudi poblacional en salut mental, el comunament anomenat estudi ECA *(Epidemiologic Catchment Area)* (Regier i cols., 1993), realitzat entre el 1980 i el 1985 a cinc estats dels Estats Units amb una mostra d'uns 20.000 subjectes participants. Molts estudis posteriors el van utilitzar com a model i just una dècada més tard apareix un segon gran estudi, el *National Comorbidity Survey* (Kessler i cols., 1994) en el qual es va utilitzar una versió millorada de la DIS, la *Composite International Diagnostic Interview* (CIDI) (World Health Organization, 1990). L'ús de la CIDI es va acabar estenent per Europa (Bijl i cols., 1998; Wittchen i cols., 1999) i la resta de països del món. Però a Europa la utilització de les entrevistes semiestructurades i per tant el fet que haguessin de ser professionals de l'àmbit de la salut mental qui les administressin, va produir que es generés una manca de recursos personals. Aquest obstacle es va poder solucionar en certa manera gràcies a l'aparició dels estudis en doble fase. Aquests estudis, incloïen una primera fase de selecció de persones amb risc per mitjà de l'ús d'un instrument de cribratge i de fàcil i ràpida aplicació. Era a la segona fase quan s'administraven les entrevistes per a la realització de diagnòstics i una de les més emprades va ser la *Schedules for Clinical Assessment in Neuropsychiatry* (SCAN) (Wing i cols., 1990) la qual segueix sent àmpliament utilitzada actualment.

Durant la dècada dels vuitanta, l'epidemiologia psiquiàtrica creix exponencialment i això va acompanyat d'una millora dels instruments de diagnòstic, del treball de camp i dels mètodes d'anàlisi estadístic utilitzats.

Els estudis epidemiològics en psicopatologia infantil i juvenil es considera que sorgeixen a partir dels estudis realitzats amb adults, i per tant parteixen d'aquesta tercera generació d'estudis presentats anteriorment. Concretament però, el que es

considera el primer estudi epidemiològic en psicopatologia infantil data de l'any 1959, i l'havien portat a terme els autors Lapouse i Monk als Estats Units. Posteriorment, es porten a terme estudis com els de Rutter a les dècades dels setanta i vuitanta, que ja són estudis amb una major uniformitat quant al mètode i que utilitzen uns millors processos d'avaluació, criteris diagnòstics i mètodes estandarditzats (Brandenburg i cols., 1990; Costello, 1989, Verhulst i Koot, 1992). Un altre treball destacat pel que fa a l'estudi més contemporani de l'epidemiologia en psicopatologia infantil, és l'anomenat estudi MECA (*Methods in Epidemiology in Children & Adolescents)* en el qual mitjançant l'administració d'entrevistes a pares de nens d'entre 9 i 17 anys, van obtenir una informació molt valuosa sobre la distribució dels trastorns mentals a la infància i a l'adolescència (Lahey i cols., 1996). A partir d'aquest, s'han anat fent d'altres contribucions a l'epidemiologia en psicopatologia infantil i juvenil al llarg del temps, fins arribar als estudis més recents que es segueixen realitzant avui en dia (Merikangas i cols., 2010a,b; Rescorla i cols., 2012; Vicente i cols., 2012).

### 2.1.1. Tipus d'estudis epidemiològics

En relació amb el temps d'avaluació existeixen dos tipus d'estudis epidemiològics: Estudis transversals i estudis longitudinals. Els estudis transversals impliquen que la presència o absència de psicopatologia i la presència o absència d'un possible factor associat, s'avalua en un mateix moment; mentre que els estudis longitudinals neixen amb la finalitat de poder realitzar l'estudi amb dades obtingudes quan hagi passat cert temps entre l'ocurrència dels factors etiològics i l'aparició dels símptomes psicopatològics. Aquest tipus d'estudis, proporcionen informació sobre el curs de cert trastorn psicopatològic en un determinat espai de temps. Un clar avantatge dels estudis longitudinals és que es pot obtenir informació sobre variacions que es poden produir al llarg del temps en un mateix individu i a més a més també es poden observar variacions entre els diferents individus. Les dades dels estudis longitudinals es poden recollir de manera prospectiva o retrospectiva (veure la Figura 1).

En els estudis retrospectius, per tal de determinar la prevalença de cert trastorn a la població, el que es fa és preguntar als subjectes sobre si en els darrers anys de la

seva vida han experimentat algun símptoma relacionat amb algun trastorn, per exemple en el cas de subjectes adults se'ls pregunta respecte a la seva infància. En aquest tipus d'estudis es creu que la dada s'estima a la baixa (Kessler i cols., 2005). D'altra banda, el mètode prospectiu implica que els investigadors segueixen una cohort representativa de subjectes en un determinat moment evolutiu, mentre que es van repetint avaluacions en diferents períodes o fases. Es considera que mitjançant els estudis prospectius, es redueix el problema que sorgeix en els retrospectius, és a dir, una infra-estimació de les dades de prevalença, i per tant les dades sobre prevalença de vida d'un determinat trastorn es consideren més representatives en el cas dels estudis prospectius (Argimon i Jiménez, 2000; Hamdi i Iacono, 2013; Moffitt i cols., 2010).

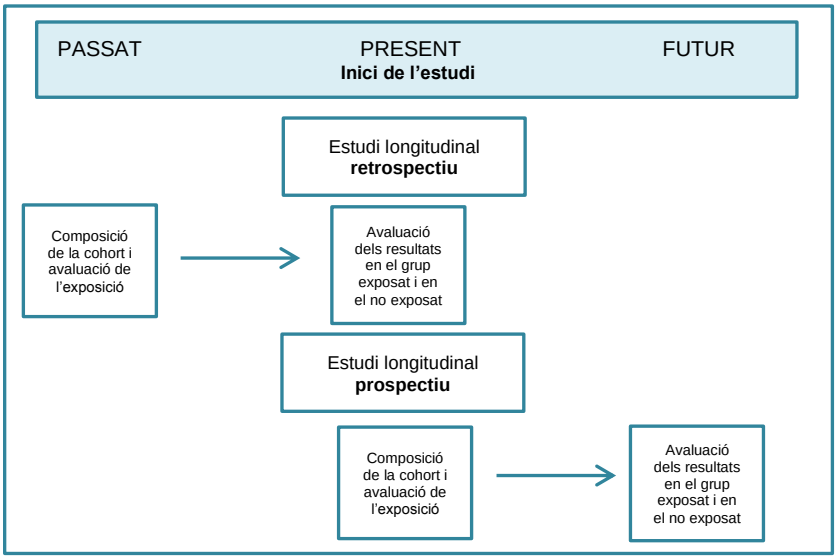


**Figura 1.** Representació gràfica de la línia del temps en un estudi longitudinal retrospectiu i en un de prospectiu. Extreta de l'article d' Euser i cols. (2009)

Els estudis longitudinals presenten gran virtuts que fan que el seu ús hagi estat de gran importància per a l'epidemiologia en psicopatologia infantil i juvenil. Aquest tipus d'estudis proporcionen dades sobre factors de risc ja que com s'ha dit, el fet que passi un temps entre les diferents mesures, permet postular una relació causal entre un esdeveniment anterior i un esdeveniment posterior. Són també

avantatjosos per a obtenir informació relacionada amb el curs d'un determinat trastorn i per a observar fenòmens com la recurrència o la remissió. També per a observar determinats canvis d'un trastorn a un altre en una època de transició com pot ser el pas de l'adolescència a l'edat adulta. A més a més que també permeten realitzar fins i tot una estimació sobre el cost-benefici d'haver aplicat o no mesures preventives. Els estudis longitudinals també tenen l'avantatge que permeten obtenir dades de prevalença en un primer temps transversal i d'incidència posteriorment. Estudiar la prevalença permet conèixer la proporció d'individus d'una determinada població, que presenten un trastorn o símptomes al llarg d'un determinat període de temps, mentre que la incidència és una dada sobre la proporció d'individus que desenvolupen un determinat trastorn o manifesten determinats símptomes, al llarg d'un període de temps i després d'haver estat considerats individus sans.

Però com tot, els estudis longitudinals també presenten algunes limitacions a banda que poden arribar a tenir un cost molt elevat, com per exemple el fet que s'utilitzin diferents informants per a la recollida de les dades (nens, pares o mestres), ús de diferents criteris diagnòstics, alguns tenen en compte mesures sobre el nivell de severitat i d'altres no, alguns investiguen prevalença de símptomes mentre que d'altres investiguen prevalença de trastorns, o bé el problema de l'ús de mostres amb subjectes de diferents edats, o també les altes taxes d'abandonament que es poden produir al llarg del seguiment, entre d'altres qüestions (Argimon i Jiménez, 2000; De Graaf i cols., 2013). Tot plegat comporta una gran limitació que presenten aquest tipus d'investigacions i és el fet que els diferents estudis són difícilment comparables entre ells; per exemple en el cas de les dades de prevalença, la varietat entre les dades obtingudes en diferents països és molt gran.

Pel que fa a l'ús de diferents criteris diagnòstics, això es deu a l'existència de diferents sistemes de classificació dels trastorns mentals. En l'àmbit de la salut mental són dos els sistemes més àmpliament utilitzats tant en la pràctica clínica com en investigació. Per una banda existeix el *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (que des del maig de 2013 es troba disponible en la seva cinquena edició; DSM-5) i que és de l'*American Psychiatric Association* (APA), per tant prové d'un enfocament més aviat Nord Americà. D'altra banda hi ha la *International Classification of Deseases* (ICD) (actualment s'utilitza la desena versió; ICD-10), amb una tradició més de caire internacional ja que va ser publicada per

l'Organització Mundial de la Salut (OMS) amb l'objectiu de promoure que es poguessin comparar a nivell internacional les dades obtingudes en diversos estudis sobre salut mental i que així els diferents clínics i investigadors realitzessin diagnòstics més unificats. Ambdós sistemes es considera que presenten una organització de tipus categorial dels diferents trastorns mentals, els quals s'agrupen en diferents categories que es defineixen per un conjunt de símptomes identificables en la pràctica clínica. Malgrat que existeix el sentiment generalitzat que no és útil tenir dos sistemes de classificació independents i amb diferències importants entre ambdós, tenir-los també pot ser molt útil per a tenir ben organitzada la informació i per a facilitar la comunicació entre professionals. Aquests són els sistemes de classificació vigents i són els que s'utilitzen per als estudis de prevalença.

Com ja s'ha esmentat, els estudis de prevalença han estat molt rellevants en el coneixement de l'epidemiologia dels trastorns tant en adults com en psicopatologia infantil i juvenil. Són el tipus d'estudis que s'han realitzat amb més freqüència. Així, són múltiples els estudis de prevalença que s'han portat a terme en diferents països i utilitzant mostres de nens i adolescents, amb la finalitat de quantificar la freqüència amb la que es produeix un determinat trastorn psicopatològic en aquest període evolutiu.

### 2.1.2. Estudis de prevalença en psicopatologia infantil i juvenil

Entre un 10 i un 20% dels nens i adolescents de tot el món, estan afectats per algun problema de salut mental. Malgrat els problemes de salut mental són considerats la causa principal de discapacitat en aquest grup d'edat i malgrat els seus efectes es prolonguen al llarg de la vida d'aquests individus, avui dia encara es considera una qüestió poc estudiada i molt descuidada, especialment en països amb nivells socioeconòmics més baixos (Kieling i cols., 2011).

Les taxes de prevalença proporcionades al llarg dels diferents estudis, presenten una gran variabilitat (1,8% - 39,4%), cosa que es pot deure a l'heterogeneïtat quant a les tècniques metodològiques emprades, o a d'altres qüestions com el fet que els factors de risc o factors protectors existents varien segons el context (Kieling i cols., 2011; Polanczyk i cols., 2007).

A continuació s'esmenten alguns estudis de prevalença que s'han realitzat tant als Estats Units com a Europa, durant els últims tres o quatre anys.

Als Estats Units els darrers estudis de prevalença que s'han realitzat són sobre prevalença d'ideació suïcida en subjectes d'entre 13 i 18 anys i s'observen taxes de fins a un 12,1% (Nock i cols., 2013). També s'ha realitzat un estudi de prevalença sobre el recentment incorporat al DSM-5: Trastorn de la desregulació disruptiva de l'estat d'ànim, s'han trobat prevalences a tres mesos d'entre un 0,8% i un 3,3% en subjectes d'entre 2 i 17 anys (Copeland i cols., 2013). S'han estudiat també els trastorns de la conducta alimentària i els resultats mostren taxes d'entre un 0,3% i un 1,6% en una mostra de subjectes d'entre 13 i 18 anys (Swanson i cols., 2011). Pel que fa als símptomes d'ansietat somàtica, Ruchkin i Schwab-Stone (2013) van observar prevalences d'entre un 20,4% i un 57,5% en subjectes amb una mitjana d'edat de 13 anys. Dos estudis importants sobre prevalença que es van publicar als Estats Units són els de Merikangas i cols. (2010a,b), un es va realitzar amb nens d'entre 8 i 15 anys i l'altre amb adolescents d'entre 13 i 18 anys. En aquest estudi s'hi mostren les prevalences a dotze mesos dels trastorns psicopatològics més comuns a les primeres etapes de la vida, concretament als resultats s'hi observen taxes de prevalença de 8,6%, 3,7%, 2,1%, 0,7% i 0,1% de trastorn per dèficit d'atenció amb hiperactivitat (TDAH), trastorns de l'estat d'ànim, trastorns de conducta, trastorn de pànic juntament amb ansietat generalitzada i trastorns de la conducta alimentària, respectivament. Pel que fa als adolescents, els trastorns d'ansietat són els que es manifesten amb una major freqüència (31,9%), seguits dels trastorns de conducta (19,1%), trastorns de l'estat d'ànim (14,3%), i trastorn d'abús de substàncies (11,4%) i la conclusió d'aquest estudi és que quatre de cada cinc joves estatunidencs, compleix criteris per almenys un trastorn mental al llarg de la seva vida, cosa que li comporta una interferència severa i un deteriorament important a la seva vida quotidiana.

En països Europeus com Suècia o Dinamarca recentment s'han estudiat les prevalences de trastorn de tics i de trastorns de l'espectre autista i s'han obtingut taxes de 0,6% de Síndrome de Tourette i 0,8% de trastorns de l'espectre autista, respectivament (Kraft i cols., 2012; Nygren i cols., 2012). En un estudi realitzat a Itàlia mostren prevalences d'un 6,5% de trastorns emocionals i d'un 1,2% de trastorns exterioritzats (Frigerio i cols., 2009). Un estudi realitzat recentment a Irlanda, en el qual van investigar la prevalença de trastorns mentals en escolars d'entre 11 i 13

anys, van observar taxes de prevalença per a qualsevol trastorn mental d'entre 27,4% i 36,8%, les quals disminueixen quan s'exclouen els diagnòstics de fòbia específica (15,4% - 31,2%) (Coughlan i cols., 2014).

A Espanya, els estudis de prevalença sobre trastorns de la conducta alimentària han estat dels que més han predominat. Els primers estudis daten de la primera meitat de la dècada dels noranta i la majoria es van realitzar mitjançant mostres d'escolars. Malgrat els avenços que es van anar produint, molts d'aquests estudis presenten diverses limitacions metodològiques que els fan difícilment comparables entre ells. Aquestes limitacions fan referència a possibles estimacions a la baixa dels percentatges de prevalença i que serien degudes a l'ús dels estudis epidemiològics en doble fase, en els que es creu que probablement molts subjectes amb un possible trastorn de la conducta alimentària, no van ser identificats en una primera fase de cribratge i per tant tampoc van ser diagnosticats posteriorment (García-Reyna i cols., 2003; Morandé i cols., 1997; Pérez-Gaspar i cols., 2000; Rojo i cols., 2003; Ruiz-Lázaro i cols., 1998; Sancho i cols., 2007). Una altra limitació és que la majoria d'aquests estudis no analitzaven els possibles factors de risc existents.

D'altres investigacions que s'han realitzat a Espanya en el camp de l'epidemiologia infantil i juvenil, són sobre la prevalença de depressió en nens (Canals i cols., 1995; Domènech i cols., 2009; Polaino-Lorente i Domènech, 1993), sobre trastorns de conducta en nens de 10 anys (Andrés i cols., 1999), trastorn bipolar (Soutullo, 2005), simptomatologia ansiosa (Romero-Acosta i cols., 2010), trastorn obsessiu compulsiu (TOC) (Canals i cols., 2012c) i sobre psicopatologia infantil i juvenil en general (Ezpeleta i cols., 2007; Gómez-Beneyto i cols., 1994; Jané i cols., 2006; Subira i cols., 1998).

Com s'ha vist, algunes investigacions es centren més en l'estudi d'algun trastorn concret i en determinar-ne la seva prevalença, curs o factors de risc, i per tant es tractaria d'estudis més específics. En canvi, d'altres estudis examinen la prevalença dels trastorns psicopatològics en general, tot i que cal dir que pel que fa a aquest darrer grup existeixen una menor quantitat d'estudis. A nivell general es considera que encara són pocs els estudis de prevalença existents.

### 2.1.3. L'estudi dels factors de risc en psicopatologia infantil i juvenil

L'estudi de l'etiologia és un dels objectius principals de l'epidemiologia en psicopatologia i els resultats obtinguts permeten aplicar mesures preventives o bé la realització d'una intervenció més eficaç. Tanmateix, es considera que la majoria del coneixement de què es disposa sobre prevenció de trastorns mentals, prové de l'aportació epidemiològica. Respecte a l'estudi dels factors de risc, segons Del Barrio Gándara (2005) s'ha de fer des de dues perspectives que es complementen entre elles. Per una banda hi hauria allò que pot resultar perjudicial (factor de risc) i per l'altra allò que pot resultar protector (factor protector). Concretament, un factor de risc és aquella circumstància que augmenta la probabilitat que aparegui un trastorn, mentre que un factor protector és aquell que disminueix la probabilitat que aparegui un trastorn (Rutter, 1985). És necessari remarcar que alguns autors creuen que s'ha de ser més precís en el llenguatge referit als factors de risc, ja que en ocasions s'utilitza indistintament junt amb el concepte de factor associat. La definició d'aquest últim implica que existeix una associació entre dues variables, sense especificar cap tipus de direcció en la relació, i en canvi un factor de risc pròpiament faria referència a un factor que precedeix el resultat (Kraemer i cols., 1997; Kraemer i cols., 2001). L'actuació de tots aquests factors genera la millor o pitjor capacitat d'afrontar els esdeveniments traumàtics, produint per tant una major o menor probabilitat d'aparició d'algun trastorn psicopatològic. Així, una situació en què per exemple es produís una manca de factors protectors i a més a més l'existència de factors de risc com una personalitat inestable, una família desestructurada o problemes en les relacions socials, suposaria un desequilibri que portaria al subjecte a esdevenir més vulnerable per a l'aparició d'algun trastorn psicopatològic. En aquest sentit, sabem que l'acumulació dels factors de risc incrementa la probabilitat que aparegui un trastorn psicopatològic concret (Del Barrio Gándara, 2005).

Existeixen una gran quantitat de factors de risc i això es pot observar en els diferents estudis, on es troba que la majoria de les alteracions psicològiques s'associen a múltiples factors de risc, tenint en compte que la majoria dels factors de risc també poden tenir més d'un efecte patològic. A més a més, poden ser de naturalesa molt diversa, podent ser biològics, psicològics o socials (Perris, 1994).

En el camp de la investigació, els estudis sobre factors de risc sovint es troben amb el problema del cost que suposaria poder considerar l'àmplia quantitat de factors de

risc possibles. S'enumeren a continuació alguns dels factors de risc més estudiats en epidemiologia en psicopatologia infantil i juvenil: el substrat genètic, problemes de salut física, l'estat nutricional, la salut física i mental dels pares, la pèrdua d'algun dels progenitors, deficiències a nivell psicosocial o en l'àmbit acadèmic, l'exposició als tòxics, el fet de ser immigrant, els desastres naturals, entre d'altres (Arun i Chavan, 2009; Benjet, 2010; Jia i cols., 2010; Li i cols., 2010; Roy i cols., 2009; Ruiz-Casares i cols., 2009; Wong i cols., 2010; Zashikhina i cols., 2007).

Tot i el desavantatge que n'existeixen múltiples i molt diversos, en el cas concret dels estudis epidemiològics en psicopatologia infantil i juvenil, l'estudi dels factors de risc ha estat fonamental per a la tasca de molts pediatres i d'altres professionals que treballen amb nens.

## 2.2. Epidemiologia dels trastorns d'ansietat

Durant molts anys, l'estudi de l'ansietat infantil es considerava que no tenia interès clínic i no s'investigava sobre els trastorns d'ansietat en aquesta etapa. Aquest fet probablement es deu a que és molt comú que en les primeres etapes del desenvolupament, els subjectes presentin símptomes d'ansietat o pors considerats transitoris i propis del desenvolupament normal dels individus (Cartwright-Hatton i cols., 2006). De fet, el primer estudi epidemiològic en psicopatologia infantil i juvenil va tenir com a objectiu l'estudi de les pors i les preocupacions infantils (Lapouse i Monk, 1959). En els darrers anys, s'ha produït una transformació gradual a mesura que s'ha demostrat que hi ha un percentatge considerable de nens i adolescents de la població que pateixen alts nivells d'ansietat. En aquests casos, i després d'una correcta avaluació, la realització d'un diagnòstic de trastorn d'ansietat està clarament justificada.

I així, és com el volum d'estudis científics que tracten aquesta qüestió ha anant creixent en els darrers 25 o 30 anys (Muris i Broeren, 2009; Rapee, 2012), malgrat actualment es considera que encara manquen estudis sobre etiologia, intervenció i avaluació dels trastorns d'ansietat en aquesta etapa (Muris i Broeren, 2009).

Són varis els estudis de prevalença que han determinat que els trastorns d'ansietat són els més prevalents durant la infància i l'adolescència. De fet, diversos autors

suggereixen que són una de les formes més primerenques de psicopatologia, ja que es considera que la infància i l'adolescència són les etapes de major risc per al desenvolupament d'aquest tipus de trastorns (Beesdo i cols., 2009; Merikangas i cols., 2010a,b; Vicente i cols., 2012). Pel que fa al patró d'inici de l'ansietat, no s'han trobat diferències destacables entre els subjectes d'ambdós sexes. El que sí que s'ha observat és que tots els trastorns d'ansietat són més freqüents en el cas del gènere femení, i que aquestes diferències entre nens i nenes es poden observar aviat, augmenten amb l'edat i s'observen en diferents estudis realitzats en diferents països (Abbo i cols., 2013; Beesdo i cols., 2009; Craske, 2003; Essau i cols., 2002; Essau i cols., 2004; Lewinsohn i cols., 1998; Muris i cols., 2002).

Referent a les taxes de prevalença, es pot observar que hi ha força diferències entre les dades que ofereixen els diversos estudis existents. Aquestes diferències, poden ser degudes a les qüestions comentades anteriorment i que com també s'ha dit, suposen un greu problema a l'hora de poder comparar les dades obtingudes. En aquest sentit, es va mostrar que les taxes de prevalença a un, tres, sis i dotze mesos, que proporcionen els diferents estudis, no són significativament més baixes que quan es té en compte la prevalença al llarg de la vida (Beesdo i cols., 2009). Els estudis indiquen que la taxa de prevalença estimada per a qualsevol trastorn d'ansietat en nens i adolescents, va del 2% al 32% aproximadament (Abbo i cols., 2013; Costello i cols., 2003; Coughlan i cols., 2014; Ford i cols., 2003; Merikangas i cols., 2010a,b). Concretament, a Espanya, s'estima que la prevalença de símptomes d'ansietat està al voltant d'un 47% (Romero-Acosta i cols., 2010).

Quant a la prevalença estimada per a cada subtipus d'ansietat, els diferents estudis realitzats amb mostres de nens i adolescents mostren taxes d'entre 0,7% i 14,1% pel que fa a la fòbia específica, entre 0,6% i 20% pel que fa a la fòbia social, entre 0,2% i 3,9% de trastorn de pànic, entre 0,4% i 6,6% d'ansietat generalitzada i entre 0,6% i 8% d'ansietat de separació (Abbo i cols., 2013; Burstein i cols., 2012; Canino i cols., 2004; Coughlan i cols., 2014; Gau i cols., 2005; Keesler i cols., 2012; Kim-Cohen i cols., 2003; Merikangas i cols., 2010a,b; Shear i cols., 2006; Wells i cols., 2006). Cal tenir en compte però, que en relació amb els diferents subtipus d'ansietat, els estudis mostren que existeix certa seqüència temporal en el sentit que cada subtipus d'ansietat acostuma a ser més freqüent en un determinat moment evolutiu que en un altre. En general, s'ha descrit que el subtipus d'ansietat que s'inicia de manera més primerenca és l'ansietat de separació i algunes fòbies específiques, com la

fòbia a certs animals i a les agulles i a extraccions de sang. En una següent etapa, és a dir, cap al final de la infància i a l'inici de l'adolescència, es produeix la incidència de la fòbia social. El trastorn de pànic, l'agorafòbia i l'ansietat generalitzada, s'acostumen a iniciar al final de l'adolescència (Beesdo i cols., 2007; Beesdo i cols., 2010; Becker i cols., 2007; De Graaf i cols., 2003; Kessler i cols., 2005; Wittchen i cols., 1999; Wittchen i cols., 2003).

En l'estudi dels trastorns d'ansietat, els estudis longitudinals que analitzen el curs natural d'aquests trastorns, presenten clars avantatges. Sobretot aquells estudis que utilitzen mostres comunitàries representatives i que realitzen valoracions en períodes potencialment de risc. En aquest sentit, hi ha estudis que parlen de l'ansietat com a fenomen transitori, o bé que es presenta de manera contínua al llarg del temps però amb fluctuacions (Last i cols., 1996; Wittchen i cols., 2000). A l'estudi de Kessler i cols. (2010), es fa referència a que el curs de l'ansietat infantil sol ser crònic-recurrent, i és que sembla que fins i tot malgrat l'aplicació de tractaments, els trastorns d'ansietat acostumen a presentar-se de forma crònica (Bruce i cols., 2005; Ramsawh i cols., 2009). També, és a partir dels estudis longitudinals que s'ha clarificat que existeixen diferents subtipus d'ansietat, amb diferents característiques associades, diferents predictors i que presenten evolucions diferents. A més a més, també s'ha produït una millora pel que fa al coneixement sobre els sistemes d'avaluació de l'ansietat, i s'ha obtingut un major coneixement sobre l'alta associació entre els símptomes d'ansietat i els símptomes depressius. La presència d'ambdós tipus de manifestacions, conjuntament amb d'altres formes de psicopatologia en nens i adolescents, pot comportar l'aparició de greus problemes a nivell psicosocial i acadèmic, com per exemple problemes pel que fa al rendiment escolar i a les relacions socials amb els iguals (Sijtema i cols., 2013).

### 2.2.1. Comorbiditat en els trastorns d'ansietat

Els trastorns d'ansietat que es donen en la infància, presenten considerables taxes de comorbiditat heterotípica, en particular amb la depressió (Costello i cols., 2004; Keenan i cols., 2009; Lamers i cols., 2011). Les taxes de comorbiditat entre ambdós trastorns se situen entre un 30% i un 75% (Essau, 2008; Lamers i cols., 2011). Altres

trastorns que presenten comorbiditats amb els trastorns d'ansietat són el TDAH, els trastorns de l'alimentació, el TOC i el trastorn d'abús de substàncies, entre d'altres (Langley i cols., 2010; Swanson i cols., 2011; Swendsen i cols., 2010; Tannock, 2000). Pel que fa a la comorbiditat homotípica, les taxes també són bastant significatives. Per exemple, a l'estudi de Kendall i cols. (2010) observen que menys d'un 25% dels subjectes participants van complir criteris tan sols per un únic trastorn d'ansietat, mentre que un 36% van complir criteris per als tres tipus de trastorns d'ansietat que van ser avaluats: ansietat de separació, ansietat generalitzada i fòbia social. En nens i adolescents procedents de mostres clíniques, la comorbiditat homotípica oscil·la entre un 18% i un 75% (Franco i cols., 2007, Kendall i cols., 2001, Kendall i cols., 2010, Last i cols., 1987, Lewinsohn i cols., 1997, Masi i cols., 2004; Viana i cols., 2008).

Són varis els factors que poden influir directament sobre la presència de comorbiditat: el gènere, el nivell socioeconòmic, l'edat d'inici dels trastorns d'ansietat o l'existència de problemes de tipus mèdic, entre d'altres (Ezpeleta i Toro, 2009; Kelly i Frosch, 2013; Kendall i cols., 2010; Leyfer i cols., 2013; Ramsawh i cols., 2011). Tanmateix, se sap que la presència de comorbiditat en aquests casos, fa que augmenti la probabilitat que els símptomes d'ansietat siguin més severs i crònics amb el pas del temps, produint un major deteriorament funcional i un pitjor pronòstic (Costello i cols., 2011; Lamers i cols., 2011; Ramsawh i cols., 2009). Pel que fa als efectes del tractament en aquests casos, en un estudi recent es va observar que nens amb un diagnòstic primari d'ansietat i que presentaven comorbiditat amb trastorns de l'estat d'ànim, eren els que mostraven majors nivells de gravetat fins i tot després del tractament (Rapee i cols., 2013). En aquest estudi també van concloure que de manera general el tractament per a l'ansietat sembla reduir els trastorns de l'estat d'ànim comòrbids, en canvi s'observen menys efectes en el cas dels trastorns exteriorizats comòrbids.

Una millor comprensió de la comorbiditat en el cas dels trastorns d'ansietat, pot comportar una millora en la comprensió i coneixement actual sobre la seva etiologia, naturalesa i tractament.

### 2.2.2. Factors relacionats i factors de risc dels trastorns d'ansietat

En primer lloc, és important esmentar que els estudis epidemiològics mostren que els trastorns d'ansietat d'aparició primerenca, són factors de risc en si mateixos per al posterior desenvolupament de trastorns depressius i/o d'altres trastorns com el trastorn d'abús de substàncies (Marmorstein cols., 2010; Swendsen i cols., 2010). A més a més, l'aparició primerenca de l'ansietat també és un factor de risc d'un pitjor curs de la malaltia, i un factor de risc de major severitat dels símptomes (Ramsawh i cols., 2011).

Són múltiples les variables que s'han determinat com a factors de risc dels trastorns d'ansietat. Per una banda, existeix un clar suport a la hipòtesi que els trastorns d'ansietat són hereditaris, és a dir, de transmissió genètica (Eley i Gregory, 2004; Franic i cols., 2010). Un gran nombre d'estudis han mostrat evidència que existeixen nivells alts de trastorns d'ansietat, entre familiars de primer grau dels subjectes amb problemes d'ansietat (Hettema i cols., 2001; Lieb i cols., 2000). De fet, donat que de manera freqüent l'ansietat i la depressió es presenten conjuntament, en ocasions els fills de pares amb símptomes depressius presenten manifestacions d'ansietat (Weissman i cols., 2006). D'altra banda, els estudis realitzats amb mostres de bessons, estimen que existeix entre un 30% i un 40% d'heretabilitat pel que fa als trastorns d'ansietat; ara bé, el que manca és acabar d'identificar els gens específics que són responsables d'aquests efectes (Hettema i cols., 2001, Trzaskowski i cols., 2013). Entre aquests estudis sobre els gens que es relacionen amb l'ansietat, un dels que més s'ha estudiat és el gen de la monoamino oxidasa A (MAOA). La monoamino oxidasa (MAO) és un enzim responsable de la degradació de neurotransmissors com la serotonina, norepinefrina i dopamina (Jacob i cols., 2005; Shih i cols., 1999). Així, s'ha vist que es produeix una millora significativa dels trastorns de l'estat d'ànim i d'ansietat, quan s'administren als subjectes fàrmacs que inhibeixen l'activitat de la MAO. Aquesta evidència, tant fisiològica com farmacològica, permet comprovar perquè el gen MAOA és un excel·lent candidat per a l'estudi de la seva possible relació com a factor de risc de l'ansietat i dels trastorns depressius (Libert i cols., 2011; Reif i cols., 2012; Tadic i cols., 2003) i també d'altres trastorns psicopatològics com el TDAH o els trastorns de l'espectre autista (Guan i cols., 2008; Nymberg i cols., 2013; Verma i cols., 2014). Les troballes en aquesta direcció, indiquen que els pacients amb trastorn de pànic presenten una alta

activitat del polimorfisme del gen MAOA, especialment en el cas dels subjectes del gènere femení (Deckert i cols., 1999). També en el cas dels subjectes del gènere femení, es troba que els alts nivells d'activitat del polimorfisme del gen MAOA s'associen amb la depressió (Rivera i cols., 2009). Així, de manera freqüent es considera que l'alta activitat del polimorfisme del gen MAOA en el cas de les noies, està relacionada amb l'ansietat, mentre que la baixa activitat en el cas dels nois està relacionada amb els comportaments impulsius i agressius (Reif i cols., 2012; Rivera i cols., 2009). Aquests resultats no s'han constatat de manera consistent a través dels diferents estudis realitzats, cosa que porta a concloure que serien necessaris més estudis i realitzats a partir de mostres més àmplies, que investiguessin aquesta qüestió (Adkins i cols., 2012; Kunugi i cols., 1999; Reif i cols., 2012). Altres gens que s'ha trobat que estan relacionats amb l'ansietat són l'SLC6A4 que és el gen transportador de la serotonina, el BDNF o factor neurotròfic derivat del cervell, el gen COMT que codifica la catecol-O-metiltransferasa que és una enzima que degrada catecolamines, i el gen GABAAα6 (polimorfismes: 5-HTTLPR, Val66Met, Val158Met i T1521C respectivament) (Arias i cols., 2012; Baumann i cols., 2013; Frustaci i cols., 2008; Lesch i cols., 1996). El problema que es produeix freqüentment pel que fa als estudis dels gens candidats a presentar associacions amb l'ansietat, és que pocs d'ells han estat replicats. Per tant, s'ha de tenir present que caldrien més estudis per a poder confirmar la validesa de les troballes. Cal dir també, que la quantitat d'estudis realitzats amb mostres de nens i adolescents, és menor que en el cas dels adults. En canvi, es considera que han proliferat molt els estudis que investiguen el substrat neurobiològic de l'ansietat mitjançant tècniques de neuroimatge (Guyer i cols., 2013). A nivell biològic, s'ha observat que les regions cerebrals que estan principalment relacionades amb l'ansietat es corresponen amb els circuits del còrtex prefrontal i dins d'aquest el còrtex orbitofrontal i el cíngol anterior, i per altra banda l'amígdala, que és l'encarregada del processament de les emocions i de reconèixer un estímul potencialment perillós. Quan l'amígdala s'activa davant un estímul que identifica com a perillós, també s'activen l'eix neuroendocrí hipotàlam-putiutaria-adrenal (HPA), el nucli parabraquial i el locus ceruleus (Breiter i cols., 1996; Guyer i cols., 2013; Likhtik i cols., 2014; Nelson i Guyer, 2011). Els neurotransmissors ajuden a la comunicació entre neurones al llarg d'aquest circuit, actuant com a missatgers químics, i els que estan implicats en l'ansietat principalment són: l'àcid-aminobutíric (GABA), la serotonina, la noradrenalina, el

glutamat i la dopamina. Les variacions en l'activació a nivell anatòmic i en l'activació dels diferents neurotransmissors, són les responsables que es produeixin els diferents subtipus d'ansietat (Kim i Gorman, 2005).

També cal fer referència als estudis que parlen del factor que engloba la interacció entre la genètica i l'ambient (Eley i Lau, 2005; Franic i cols., 2010). Com a factor relacionat amb l'ambient o l'entorn dels individus, s'han realitzat estudis sobre els esdeveniments vitals. Així, esdeveniments considerats traumàtics o negatius, prediuen l'aparició posterior de trastorns d'ansietat i també de trastorns depressius (Allen i cols., 2008; Perkonigg i cols., 2000; Tiet i cols., 2001); entenent com a esdeveniments traumàtics que es poden produir a la vida d'un infant, els següents: la pèrdua d'un progenitor, el divorci dels progenitors, la mort d'un membre de l'entorn social del subjecte, viure una situació d'humiliació, entre molts d'altres.

També, variables relacionades amb la personalitat s'ha vist que poden actuar com a factors de risc dels trastorns d'ansietat. Diferents autors han comprovat que factors relacionats amb l'estil temperamental dels subjectes, com seria el cas de la inhibició conductual, estan altament relacionats amb l'increment de la probabilitat de desenvolupar un trastorn d'ansietat (Fox i cols., 2005). La inhibició conductual és una dimensió temperamental que predisposa al nen a reaccionar amb ansietat o por, cap a situacions o persones que no li resulten familiars. En aquest sentit, cal remarcar que inhibició conductual no és el mateix que els constructes fòbia social o vergonya, però sí que és un concepte que hi està altament relacionat i que pot formar part de l'espectre de l'ansietat social (Ballespí i cols., 2012; Muris i cols., 2011; Schneier i cols., 2002). De fet, la inhibició conductual es troba generalment associada amb l'ansietat i la depressió, i més concretament, sovint precedeix l'aparició de la fòbia social (Essex i cols., 2010; Muris i cols., 2011; Rotge i cols., 2011). Per tant, s'ha de prestar especial atenció a aquells nens que presenten dificultats destacables a l'hora de relacionar-se amb els iguals o que es mostren altament inhibits davant situacions que per ells són excepcionals, subjectes amb hipersensibilitat emocional, en aquests casos és possible que aquests trets es mantinguin estables al llarg de la vida i per tant intervenir ràpidament pot evitar que el problema s'acabi transformant en problemes d'ansietat greus.

A més a més, hi ha una sèrie de variables sociodemogràfiques que s'ha demostrat que també actuen com a factors de risc en el cas de l'ansietat. Dins d'aquestes el

gènere; s'ha observat que ser nena és un factor de risc per al desenvolupament de trastorns d'ansietat (Costello i cols., 2003), també cal considerar que aquest trastorn es produeix amb major freqüència en el cas del gènere femení. Pel que fa al nivell educatiu, són varis els estudis que han trobat unes majors taxes de trastorns d'ansietat, entre els subjectes que presenten menors nivells educatius (Van Ameringen i cols., 2003; Wittchen i cols., 1998). En aquest sentit, és possible que els subjectes s'angoixin davant la idea que no poden arribar on arriben els altres pel que fa a les tasques escolars i també pot existir certa angoixa a les situacions d'avaluació. D'aquesta manera, és possible que s'acabi veient afectada l'autoestima, l'adquisició d'autonomia, el nivell de motivació i les relacions socials, a banda del rendiment acadèmic. Inclús el nivell educatiu dels progenitors és un factor de risc d'ansietat en els seus descendents, en concret s'ha observat que aquesta variable està relacionada amb la persistència i la gravetat dels símptomes (McLaughlin i cols., 2011). Així, uns progenitors amb baix nivell educatiu probablement seran uns pares que no podran oferir tanta ajuda als seus fills a l'hora de realitzar les tasques escolars, o bé no es sentiran tan còmodes en un ambient escolar. També hi ha estudis que suggereixen que l'estil parental pot actuar com un factor de risc. Concretament, un estil parental sobre-protector o un estil parental contrari a aquest, és a dir, més negligent, s'ha vist que està altament associat amb taxes significatives de fòbia social en els nens (Knappe i cols., 2009). En aquesta línia, en un estudi que s'ha publicat recentment, es va observar que en un període de transició com és l'inici de l'adolescència, els subjectes esdevenen més vulnerables per desenvolupar un determinat trastorn d'ansietat quan el vincle amb els seus progenitors ha estat de tipus insegur (Esbjorn i cols., 2012). Probablement es tractarà de nens que seran més insegurs podent arribar al sentiment que per si sols no poden fer les coses correctament, qüestió que pot afectar també a la seva autoestima, nivell d'autonomia personal i a les seves relacions amb els altres. Un altre factor significativament relacionat amb l'ansietat infantil, s'ha vist que és l'afectivitat negativa per part de la mare i l'estrès parental (Pahl i cols., 2012; Van Oort i cols., 2011). Una altra variable sociodemogràfica seria el nivell socioeconòmic familiar. En diversos estudis s'ha trobat que existeix una relació entre el nivell d'ingressos de la família i l'aparició posterior de manifestacions d'ansietat (McLaughlin i cols., 2011). Així, un nivell d'ingressos familiar baix està relacionat amb l'aparició dels trastorns d'ansietat (Van Oort i cols., 2011). En termes generals, cal

tenir en compte que s'han de considerar tots els elements que formen part de l'entorn del subjecte. Els valors, les expectatives o els aspectes socioeconòmics que regeixen un determinat context, es poden relacionar amb l'aparició o agreujament dels símptomes psicopatològics que poden aparèixer al llarg del desenvolupament.

Els estudis que han investigat la qüestió dels factors de risc dels trastorns d'ansietat, són els que han contribuït a que s'obrissin perspectives relacionades amb la intervenció primerenca i la prevenció, a fi d'evitar un augment significatiu de les taxes d'aquests trastorns mentals en un futur.

## 2.3. Epidemiologia del TOC

Lligat amb els trastorns d'ansietat, històricament el TOC ha estat classificat dins d'aquesta categoria. Els símptomes obsessius que caracteritzen el TOC, produeixen alts nivell d'ansietat que sovint porten al subjecte a la realització de les compulsions per tal d'alleujar-la. Tal i com es veurà més endavant, la presència conjunta dels símptomes d'ansietat i dels símptomes del TOC és un fet que es produeix amb una alta freqüència.

Des de fa unes dècades, ja no es té la concepció que el TOC infantil i juvenil no existeix, i s'ha produït un augment exponencial del coneixement sobre la seva clínica, bases biològiques, tipus de tractaments, etc. Però pel que fa als estudis de prevalença, curs o estudis relacionats amb l'impacte que aquest causa a la vida dels qui el pateixen, les dades continuen sent escasses. A més, alguns investigadors postulen que pot ser que sovint el TOC es trobi infra-diagnosticat per manca de detecció en alguns casos. Tal fet es deu a que aquest trastorn pot implicar un secretisme per part del subjecte en percebre els seus símptomes com a quelcom que li causa sentiments de vergonya o incomoditat, existint així una dificultat important per a obtenir dades epidemiològiques exactes. En el cas dels nens, també pot passar que es produeixi una manca de consciència de la malaltia (Turner i Swearer, 2010).

Com ja s'ha dit, pel que fa a les dades de prevalença de TOC en nens i adolescents, es considera que són pocs els estudis existents. De fet, en determinats grups d'edat com per exemple entre els 8 i els 15 anys, la manca de dades de

prevalença encara és més notable. El primer estudi de prevalença de TOC en nens va ser Europeu, el van realitzar concretament a Anglaterra, i el van conduir Rutter i cols. (1970) qui varen obtenir unes dades de prevalença d'entre un 0,3% i un 0,4% en subjectes d'entre 10 i 11 anys. En síntesi, pel que fa a la resta d'estudis de prevalença existents, realitzats en diferents països, amb subjectes de diversos rangs d'edat, i mitjançant l'ús de diferents eines metodològiques, les prevalences de TOC en nens i adolescents oscil·len entre un 0,1% i un 4% (Brynska i Wolanczyk, 2005; Canals i cols., 2012c; Coughlan i cols., 2014; Douglass i cols., 1995; Flament i cols., 1988; Heyman i cols., 2001; Lewinsohn i cols., 1993).

L'edat d'inici ha estat també una qüestió àmpliament investigada. El principal problema que s'ha produït en aquest camp, és l'arbitrarietat existent entre les diferents definicions sobre què implica TOC d'inici primerenc i TOC d'inici tardà (Anholt i cols., 2014). Manca unanimitat pel que fa a l'establiment d'un punt de tall per a cada concepte. A l'estudi recent d'Anhold i cols. (2014) s'ha definit un punt de tall que correspon a l'edat de 20 anys. Per tant, si els símptomes TOC s'inicien per sota d'aquesta edat es considerarà TOC d'inici primerenc, i si pel contrari s'inicien després dels 20 anys d'edat, es considerarà TOC d'inici tardà. Per una altra part, estudis realitzats amb àmplies mostres van observar que l'edat mitjana d'inici del TOC són els 15 anys (De Luca i cols., 2011) i que és infreqüent que el TOC s'iniciï després dels 30 anys d'edat (Grant i cols., 2007). Una altra proposta pel que fa a l'edat d'inici i que va ser àmpliament acceptada, va ser la realitzada per Delorme i cols. (2005). Aquests autors fan referència a una distribució bimodal (barreja de dues distribucions gaussianes) on el primer pic coincideix amb el TOC d'inici primerenc i situa l'inici del trastorn als 11,1 ± 4,1 i el segon pic coincideix amb el TOC d'inici tardà i situa l'edat d'inici del trastorn entorn als 23,5 ± 11,1 anys.

Determinar totes les qüestions corresponents a l'edat d'inici d'aquest trastorn, es considera important per a la seva tipificació. En aquest sentit, són molts els estudis que han trobat força característiques que són pròpies del TOC d'inici primerenc i que poden estar indicant que aquest pot ser un subtipus específic de TOC. En són exemples la seva associació amb una major severitat dels símptomes (Do Rosario-Campos i cols., 2001; Lomax i cols., 2009), amb la presència de símptomes relacionats amb superstició (Millet i cols., 2004), amb la presència de tics, trastorns d'ansietat i trastorns de la conducta (Do Rosario-Campos i cols., 2001; Eichstedt i Arnold, 2001; Geller

i cols., 1996; Geller i cols., 2001; Narayanaswamy i cols., 2012), i l'associació amb el gènere masculí (Cherian i cols., 2014; De Mathis i cols., 2011; Fontenelle i cols., 2003; Narayanaswamy i cols., 2012; Taylor, 2011). A més a més, existeix certa controvèrsia pel que fa als efectes del tractament, en funció de si es tracta de TOC d'inici primerenc o TOC d'inici tardà. Mentre alguns autors suggereixen que els subjectes amb TOC d'inici primerenc no milloren tant en resposta al tractament (Erzegovesi i cols., 2001), d'altres conclouen que no hi ha diferència entre ambdós grups pel que fa a la resposta al tractament (Fontenelle i cols., 2003; Millet i cols., 2004).

El gènere és un factor important a tenir en compte en l'avaluació de pacients amb TOC (De Mathis i cols., 2011), i també és important per a la investigació del mateix. De fet, donat que el TOC és considerat un trastorn heterogeni, conèixer diferències a nivell de gènere també pot ajudar a identificar alguns subgrups homogenis. A banda, l'estudi d'aquestes diferències també pot contribuir a la clarificació dels factors etiològics, coneixement relacionat amb la presentació i el curs del trastorn, i al desenvolupament de nous tractaments (De Mathis i cols., 2011). Als estudis realitzats amb mostres d'adults s'ha comprovat que les majors prevalences es donen en el cas del gènere femení (Fontenelle i cols., 2004). En referència als subjectes que es troben a l'etapa de l'adolescència, sembla que també són les nenes les que presenten el trastorn amb una major freqüència (Brynska i Wolanczyk, 2005; Maggini i cols., 2001; Ruscio i cols., 2010). En aquest sentit, es considera que és a partir de l'adolescència i en endavant que les diferències entre ambós gèneres es fan més evidents (Walitza i cols., 2011). Finalment, si ens remuntem a les etapes més primerenques del desenvolupament, s'ha observat que la majoria dels casos d'inici primerenc de TOC es produeixen en subjectes del gènere masculí. Concretament, algunes dades confirmen que una quarta part dels nois experimenten l'inici abans dels 10 anys d'edat. En canvi, en el cas del gènere femení s'ha vist que en la majoria dels casos el TOC s'inicia durant l'adolescència (Ruscio i cols., 2010). Però convé destacar que en general, existeix una gran controvèrsia entre els estudis que tenen per objectiu determinar si el TOC és un trastorn que afecta a una major proporció de subjectes d'un o altre gènere (Fontenelle i Hasler, 2008; Heyman i cols., 2001; Masi i cols., 2004; Valleni-Basile i cols., 1994). Així, l'expressió fenotípica del trastorn pot presentar variacions en funció del gènere, com es produeix en el cas dels diferents tipus d'obsessions. Mentre que les obsessions relacionades amb

l'ordre i la simetria s'ha vist que són més freqüents en el cas del gènere masculí, les obsessions de contaminació i neteja apareixen més relacionades amb el gènere femení (Masi i cols., 2010). Pel que fa als adults, també les obsessions relacionades amb la contaminació i la neteja són més pròpies en el cas de les dones, mentre que les obsessions de tipus sexual o religiós s'ha vist que són més freqüents en el cas dels homes (Cherian i cols., 2014; Labad i cols., 2008).

Els treballs d'investigació més recents, segueixen fent referència a la manca d'estudis prospectius que existeixen relacionats amb el curs del TOC (Fineberg i cols., 2012; Micali i cols., 2010). En general, la majoria dels estudis suggereixen que el TOC presenta un curs crònic, és a dir, evoluciona de forma continuada, tot i que no sempre es manifesta amb la mateixa intensitat. Concretament se sol dir que presenta fluctuacions i és episòdic. En infants, inclús s'ha vist que en alguns casos el TOC esdevé subclínic amb el pas del temps (Stewart i cols., 2004). Per altra banda, en un estudi recent realitzat amb una mostra clínica d'adults, van observar que un 61,7% dels participants van complir criteris de cronicitat del TOC, indicant que la cronicitat és més una regla que una excepció en mostres clíniques (Visser i cols., 2014). A més a més van observar que els pacients que presentaven un curs crònic, presentaven una major severitat dels símptomes de TOC, més comorbiditat, un inici més primerenc i una major freqüència de símptomes relacionats amb la neteja i la contaminació, i la simetria i l'ordre. Per tant, un punt important és el fet que es necessiten un major nombre d'estudis relacionats amb el curs d'aquest trastorn, i en especial calen estudis realitzats amb mostres comunitàries àmplies. És necessària una determinació més precisa de la patogènesi del TOC.

### 2.3.1. Comorbiditat en el TOC

El TOC no és un trastorn que acostumi a presentar-se de manera aïllada, sinó que habitualment es manifesta de manera comòrbida amb d'altres trastorns i/o símptomes. De fet, entre un 60% i un 80% dels nens i adolescents amb TOC presenten un o més trastorns psicopatològics comòrbids com el TDAH, trastorns d'ansietat, o trastorns de la conducta alimentària (Geller, 2006; Kim i cols., 2012). Com ja s'ha dit, són molts els factors que poden estar relacionats i que influeixen en la

presència de comorbiditat. A més a més, els patrons de comorbiditat poden variar notablement entre els diferents individus (Murphy i cols., 2010).

La comorbiditat pot actuar emmascarant el diagnòstic de TOC, pot influir en l'evolució del mateix i en la resposta al tractament. Per exemple, una llarga durada del TOC s'ha relacionat amb l'aparició d'humor depressiu i de fòbia social (Diniz i cols., 2004). També s'ha observat, que si existeix comorbiditat la resposta al tractament és més baixa i augmenta el percentatge de recaigudes a posteriori del tractament (Farrell i cols., 2012; Geller i cols., 2003; Krebs i Heyman, 2010; March i cols., 2007). En un estudi recent, s'ha suggerit que especialment en aquells casos en què el subjecte presenta símptomes obsessius comòrbids amb trastorns com l'ansietat o la depressió, el tractament combinat (fàrmacs i teràpia cognitiu-conductual) és el que mostra millors resultats (Sánchez-Meca i cols., 2014), essent també molt important la implicació dels pares per a l'efectivitat del tractament. Però com s'anava dient, en aquests casos la presència de comorbiditat comporta un clar impacte negatiu sobre la salut dels subjectes i a nivell psicosocial (Fineberg i cols., 2013a,b).

Una altra qüestió destacable, està relacionada amb la importància de determinar quin és el trastorn que es produeix abans. És a dir, s'ha vist que per exemple en casos en els quals el TDAH es va iniciar abans que el TOC, el subjecte té unes majors probabilitats de patir un trastorn per abús de substàncies en els propers anys, i també són subjectes que acostumen a presentar un pitjor curs del TOC. De la mateixa manera, s'ha comprovat que els subjectes que van manifestar un trastorn d'ansietat de separació amb anterioritat al TOC tendien a patir, en un futur, trastorn d'estrès posttraumàtic amb una major probabilitat, a més a més de presentar també una major vulnerabilitat per patir múltiples trastorns d'ansietat (De Mathis i cols., 2013). Segons aquests autors, manquen estudis que hagin investigat l'efecte de l'edat d'inici de cada trastorn que es presenta comòrbid amb el TOC, sobre l'evolució del mateix. També van observar que a la seva mostra, el trastorn que de manera més primerenca es presentava associat al TOC era l'ansietat de separació, seguit del TDAH i dels tics.

La comorbiditat del TOC amb la depressió ha estat àmpliament estudiada. S'ha comprovat que aquest tipus de comorbiditat es produeix de manera molt freqüent i que resulta de gran impacte en el curs del TOC, mostrant també efectes sobre el

tractament (Farrell i cols., 2012; Geller i cols., 2003; Peris i cols., 2010; Storch i cols., 2008; Storch i cols., 2012). Tot i que existeixen algunes controvèrsies, molts estudis estan d'acord en suggerir que els símptomes depressius apareixen després del TOC, pel desgast que es produeix degut a la severitat dels seus símptomes (Abramowitz i cols., 2007). En aquesta direcció, en un estudi recent s'ha observat que centrar-se en el tractament del TOC, disminueix els símptomes depressius associats (Meyer i cols., 2013).

En síntesi, la comorbiditat en el TOC és un factor clínicament rellevant ja que es pot associar a un patró específic de vulnerabilitat, amb una major cronicitat del TOC i un curs amb una major gravetat i conseqüències negatives per a la vida diària del subjecte. En aquest sentit, el diagnòstic i tractament de tots els trastorns comòrbids, és una qüestió molt important. Metges, psicòlegs i d'altres professionals, han de tenir present la possibilitat que un trastorn no es presenti de manera aïllada, per tal d'aplicar el tractament més adequat.

### 2.3.2. Factors relacionats i factors de risc del TOC

Molts autors afirmen que la complexa etiologia del TOC és un camp poc explorat. Però en termes generals es pot dir que entre les causes del TOC s'hi inclouen tant factors genètics com ambientals i també la interacció entre ambdós.

Recentment, les causes genètiques del TOC han estat motiu d'estudi per a molts investigadors i malgrat s'han detectat alguns gens que són candidats a estar altament relacionats amb el TOC, encara es considera que aquest camp és àmpliament desconegut i que calen més estudis en aquesta direcció (Mathews i cols., 2012). Concretament, fins al 2010 s'havien realitzat 80 estudis d'associació genètica, abarcant l'estudi de fins a 24 gens candidats (Pauls, 2010).
En termes molt generals, els estudis mostren una relació entre el TOC i els polimorfismes vinculats amb el sistema serotoninèrgic (5-HTTLPR i HTR2A). També s'ha vist que només en el cas del sexe masculí, hi ha una relació amb polimorfismes implicats en la modulació de les catecolamines (COMT i MAO). Els estudis també mostren algunes tendències relacionades amb polimorfismes associats amb el

glutamat (rs30878779) i amb la dopamina (DAT1 i DRD3) (Taylor, 2013). D'altra banda, Pauls (2010) va suggerir que tot i que s'estan realitzant molts estudis sobre genètica del TOC, en especial estudis d'associació, calen estudis realitzats amb mostres molt més grans, també cal replicar-los per poder obtenir conclusions amb més certesa i cal que es realitzin en el si d'equips multidisciplinaris. A més a més conclou que, la complexitat fenotípica del TOC implica que no tots els gens candidats estudiats seran l'única causa del TOC, perquè tot i que potser sí que estaran relacionats amb el seu inici, severitat o persistència, probablement no seran l'única causa sense comptar també amb la presència d'altres gens de risc. De fet, un dels models més acceptats és el relacionat amb la hipòtesi poligenètica, que suggereix que són múltiples gens els que realitzen petites contribucions a mode de factors de risc per a desenvolupar el trastorn (Taylor, 2013).

El gen SLC6A4 (polimorfisme 5-HTTLPR) ha estat un dels més estudiats pel que fa a la seva possible vinculació amb l'aparició del TOC (Bloch i cols., 2008; Hu i cols., 2006; Voyiaziakis i cols., 2011). L'SLC6A4 actua com un transportador de serotonina des de l'espai extracel·lular (Nordquist i Oreland, 2010). En aquest sentit, alguns estudis han mostrat que concretament el TOC d'inici tardà, s'associa amb una baixa disponibilitat del transportador de serotonina al cervell (Hasselbalch i cols., 2007; Hesse i cols., 2011) la qual cosa també és un indicador de la relació existent entre aquest gen i el TOC. D'altra banda, pel que fa al substrat neurobiològic del TOC els treballs d'investigació fan referència a l'existència d'una desregulació a nivell dels sistemes cerebrals cortico-estriats, circuits neuronals que connecten els ganglis basals, el tàlem i el còrtex (Haber, 2003). Els estudis de neuroimatge mostren que en les persones amb TOC el còrtex orbito frontal, el cíngol anterior i l'estriat es mostren hiper-activats, i en aquest sentit s'ha demostrat que el tractament disminueix aquests nivells d'activació (Friedlander i Desrocher., 2006; Rotge i cols., 2008). Concretament, en el cas dels nens i adolescents es va observar a través d'imatges obtingudes amb ressonància magnètica funcional, que els pacients amb TOC abans de prendre la medicació presentaven en general uns majors nivells d'activitat cerebral. Els ganglis basals, còrtex fronto-parietal i la circumvolució frontal mitjana bilateral es presentaven altament activats, mentre que després del tractament s'observava una disminució de l'activitat, la qual era més significativa pel que fa a la ínsula esquerra i al putàmen esquerra (Lázaro i cols., 2008). En relació amb el volum

de la substància blanca i de la subtància gris, s'han observat alteracions pel que fa als pacients amb TOC, però aquestes milloren amb els fàrmacs (Chen i cols., 2013a; Kim i cols., 2001; Lázaro i cols., 2009; Riffkin i cols., 2005; Yoo i cols., 2007). A nivell dels neurotransmissors, la serotonina està implicada en la fisiopatologia del TOC, i això s'ha confirmat quan amb l'ús de fàrmacs com els inhibidors de la recaptació de la serotonina, els símptomes del TOC han disminuït (Bloch i cols., 2006). Diferents estudis sobre neuroquímica han demostrat que el TOC està vinculat amb canvis en el sistema modulador de la serotonina i de la dopamina, així doncs obtenir més informació sobre aquestes alteracions és d'especial interès per a l'àmbit de la farmacologia (Karck i Pogarell, 2011). D'altres estudis també s'han referit al paper de l'oxitocina en els símptomes TOC (Leckman i Herman, 2002) o al paper del glutamat (Wu i cols., 2012). En altres termes, se sap que el TOC també pot estar causat per una resposta autoimmunològica a una infecció associada a l'estreptococ; el trastorn neuropsiquiàtric associat a l'estreptococ es coneix amb el seu acrònim PANDAS (*Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococci*) (Swedo i cols., 1998).

Pel que fa als factors ambientals, existeixen molts estudis que analitzen una àmplia varietat de factors. Entre d'altres, el TOC s'ha relacionat en més o menys mesura amb experiències adverses a nivell prenatal, perinatal o post-natal (Grisham i cols., 2011), estacionalitat en el moment del naixement (Kovalenko i cols., 2000), o l'ordre en el naixement; per exemple Kayton i Borge (1967) van comprovar que existien majors taxes de manifestacions TOC en nens que eren el primer fill o en fills únics. També, les possibles complicacions durant l'embaràs podrien estar relacionades amb el TOC (Vasconcelos i cols., 2007). Un altre factor seria el fet d'haver viscut algun esdeveniment traumàtic (Guerrero i cols., 2003; Valleni-Basile i cols., 1996). A més a més, en un estudi recent es va concloure que si el TOC és desencadenat per un factor estressant precipitant, sembla que el patró de manifestacions clíniques del trastorn és diferent (Real i cols., 2011). D'altres estudis han investigat la relació entre el TOC i algunes variables sociodemogràfiques i per exemple en alguns d'ells s'ha mostrat que el gènere masculí pot ser un factor de risc d'inici primerenc de TOC, com ja s'ha dit anteriorment (Fontenelle i cols., 2003; Walitza i cols., 2011). També, el nivell socioeconòmic familiar ha estat una variable àmpliament estudiada, però els resultats dels diferents estudis estan en desacord quant a la seva relació negativa o

positiva amb el TOC (Fontenelle i Hasler, 2008; Heyman i cols., 2001; Van Oort i cols., 2011). D'altres variables que també s'han explorat són l'estat civil de les persones amb TOC, el nivell educatiu o laboral i la raça o ètnia, la personalitat, el temperament, el nivell cognitiu dels subjectes amb TOC i el dels seus familiar, entre d'altres (Breslau i cols., 2006; Cherian i cols., 2014; Crino i cols., 2005; Grabe i cols., 2000; Mohammadi i cols., 2004; Nestadt i cols., 1994); cal dir que els resultats obtinguts als diferents estudis mostren força variabilitat.

# 3.Objectius i hipòtesis

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 3. Objectius i hipòtesis

## 3.1. Objectiu i hipòtesi generals

L'objectiu d'aquesta tesi ha estat l'estudi prospectiu de la simptomatologia d'ansietat i obsessiva-compulsiva en població escolar, així com l'estudi de factors de risc i associats a aquestes patologies.

La hipòtesi principal del treball va ser que tant els símptomes d'ansietat com els símptomes obsessius-compulsius tenen un curs crònic a l'etapa estudiada i poden alterar el funcionament psicosocial i acadèmic en l'adolescent.

### 3.1.1. Objectius i hipòtesis específics

**1-** Investigar la capacitat predictiva i l'associació de característiques psicopatològiques i sociodemogràfiques en relació al diagnòstic de TOC, tenint en compte dos nivells de severitat del mateix.

- **a.** Esperem trobar una associació entre símptomes emocionals i el TOC, independentment del nivell de severitat del diagnòstic.
- **b.** En aquesta edat pensem que els símptomes conductuals poden també estar associats al TOC.
- **c.** No esperaríem trobar relacions entre les variables sociodemogràfiques i el TOC.

**2-** Conèixer la taxa de prevalença, persistència, recurrència i incidència dels símptomes obsessius-compulsius segons dos nivells de severitat.

- **a.** Esperem obtenir taxes de persistència i recurrència de símptomes obsessius-compulsius considerables, per tant creiem que l'espectre obsessiu-compulsiu manté una cronicitat.

**3-** Explorar els factors psicopatològics que poden predir les manifestacions obsessives-compulsives a la última fase de seguiment.

- **a.** Creiem que la presència de símptomes obsessius-compulsius i d'ansietat previs, serà predictor de la simptomatologia obsessiva-compulsiva a llarg termini, independentment del nivell de severitat d'aquesta simptomatologia.

**4-** Conèixer, segons el sexe, la taxa de prevalença, persistència, recurrència i incidència dels diferents tipus de símptomes d'ansietat al llarg de l'estudi.

- **a.** Esperem trobar uns percentatges alts de cronicitat en els símptomes d'ansietat.
- **b.** Els símptomes d'ansietat seran més prevalents, persistents i incidents en el sexe femení.
- **c.** Esperem trobar diferent evolució al llarg del període estudiat pel que fa als diferents tipus de símptomes d'ansietat.

**5-** Investigar la coexistència entre símptomes psicopatològics i l'ansietat crònica.

- **a.** La cronicitat dels símptomes d'ansietat estarà relacionada amb la presència de més símptomes psicopatològics associats.

**6-** Estudiar la interferència acadèmica i social en els adolescents amb ansietat persistent.

**a.** La cronicitat dels símptomes d'ansietat estarà relacionada amb alteracions del funcionament psicosocial i acadèmic de l'adolescent.

**7-** Explorar la capacitat predictiva de símptomes emocionals previs, característiques sociodemogràfiques i antropomètriques, sobre l'ansietat persistent.

**8-** Investigar si els símptomes d'ansietat i depressius previs, prediuen el rendiment acadèmic de l'adolescent tot i controlant les variables sociodemogràfiques i el TDAH.

**a.** Pensem que el rendiment acadèmic dels adolescents pot estar afectat per la presència prèvia de simptomatologia d'ansietat i depressió. Tanmateix també esperem observar la influència negativa del TDAH sobre el rendiment acadèmic dels adolescents.
**b.** Esperem trobar una relació entre l'alt nivell socioeconòmic de les famílies i l'adequat rendiment acadèmic dels subjectes.

**9-** Explorar la possible associació entre els al·lels del polimorfisme del gen MAOA (MAOA-uVNTR) i els símptomes d'ansietat i altres símptomes psicopatològics.

**a.** Pensem que la relació entre els al·lels del polimorfisme del gen MAOA i la presència de psicopatologia, estarà mediada pel gènere dels subjectes i la influència de factors de l'entorn.
**b.** Esperem observar que els subjectes del sexe masculí amb una baixa activitat del polimorfisme del gen MAOA, tinguin més problemes de conducta; i que els subjectes del sexe femení amb una alta activitat del polimorfisme, presentin més problemes emocionals.

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 4.Mètode

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UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 4. Mètode

## 4.1. Disseny de l'estudi

Per a portar a terme l'estudi que es presenta en aquesta tesi doctoral, es va realitzar un estudi amb un disseny longitudinal prospectiu. En un primer moment el disseny de l'estudi va ser transversal en doble fase i va consistir en una primera fase de cribratge de simptomatologia emocional, que va permetre la posterior selecció d'una mostra de subjectes amb risc i una mostra de subjectes control (segona fase). La realització d'una tercera fase de seguiment, suposa que el disseny de l'estudi passi a ser longitudinal prospectiu en tres fases (veure la Figura 2).

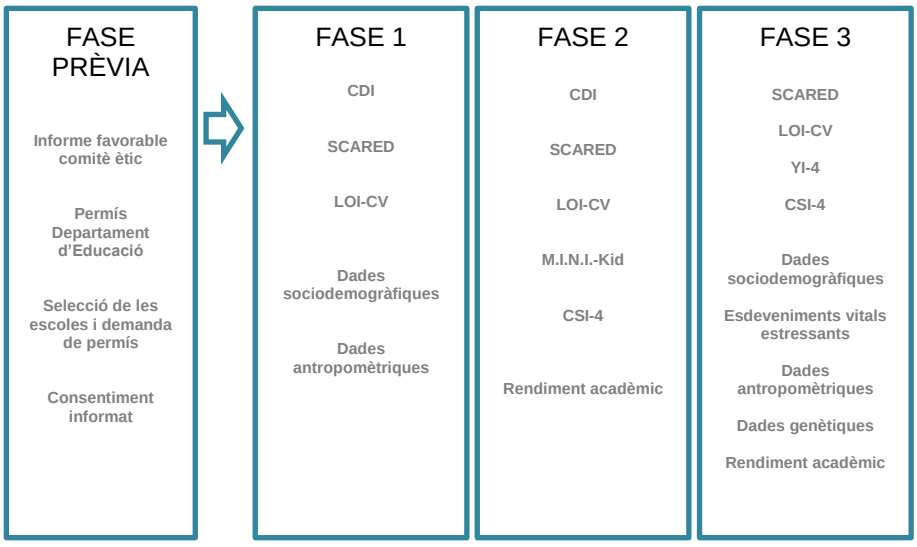


**Figura 2.** Disseny de l'estudi

## 4.2. Participants

Un total de 2.023 subjectes de quart, cinquè i sisè de primària procedents de 13 escoles (7 escoles públiques i 7 escoles concertades) de la ciutat de Reus (ciutat espanyola situada a la província de Tarragona, Catalunya) varen ser convidats a participar a un estudi epidemiològic de trastorns d'ansietat i depressius. L'estudi va constar de tres fases. A la primera fase hi varen participar 1.514 subjectes (720 nens i 794 nenes) d'entre 8 i 12 anys d'edat (M=10,23; DE=1,23).

Un 39,5% dels nens pertanyien a famílies amb un baix nivell socioeconòmic, un 42,5% a famílies amb un nivell socioeconòmic mig, i un 18% a famílies amb un alt nivell. Un 87,5% de la mostra eren subjectes nascuts a l'Estat Espanyol (la majoria d'ells a Catalunya) i un 85,9% pertanyien a famílies nuclears. Després d'haver administrat qüestionaris de cribratge a la primera fase, 562 subjectes (254 nens i 308 nenes) varen ser seleccionats com a membres d'un grup de risc de trastorns d'ansietat i/o depressius (n=405; 72,1%) o com a membres d'un grup control sense risc (n=157; 27,9%). Els participants del grup control van ser subjectes amb les mateixes característiques pel que fa a l'edat, gènere i tipus d'escola que els del grup de risc.

Dos anys després, els 562 subjectes participants a la segona fase van ser convidats a participar a la tercera fase de seguiment de l'estudi. 242 subjectes (95 nens i 147 nenes) amb una mitjana d'edat de 13,52 (DE=0,94) van entregar el consentiment informat degudament signat pels pares i van formar la mostra de seguiment a la tercera fase. No es van trobar diferències estadísticament significatives entre els subjectes que van participar a la tercera fase i els que van rebutjar participar-hi, pel que fa a les variables psicopatològiques (ansietat, depressió i TOC), ni pel que fa a les variables sociodemogràfiques (gènere, lloc de naixement i tipus de família), a excepció de diferències pel que fa al nivell socioeconòmic; la taxa d'abandonament va ser major en el cas dels participants provinents de famílies amb nivells socioeconòmics més baixos, en comparació amb els subjectes amb nivells socioeconòmics mitjos i alts ($\chi^2_{2.561}$=13,557; p=0,001).

## 4.3. Instruments

La versió espanyola del ***Leyton Obsessional Inventory-Child Version Survey*** (LOI-CV) (Berg i cols., 1988): qüestionari autoinformat que consta de 20 ítems que tenen per objectiu avaluar la presència o absència (podent contestar a cada ítem SÍ/NO) d'un determinat nombre de preocupacions i conductes obsessives. Cada ítem inclou una part on els subjectes avaluen el grau d'interferència que aquell símptoma els hi causa en tots els casos en els que ha marcat "SÍ". Aquest apartat està format per una escala on s'hi pot puntuar de 0-3 (no interfereix – interfereix molt). La versió espanyola del LOI-CV va ser validada (Canals i cols., 2012b), comprovant-se que és una eina adequada com a instrument de cribratge per a avaluar símptomes TOC en nens i adolescents. La versió espanyola també va mostrar tenir una bona consistència interna (α=0,90) i està formada per tres factors anomenats: **ordre/comprovació/neteja** (7 ítems; α=0,82), **preocupació obsessiva** (7 ítems; α=0,81), **superstició/compulsió mental** (6 ítems; α=0,77).
És important tenir en compte que s'han considerat dos tipus de puntuacions al LOI-CV, es defineixen tot seguit:

> PUNTUACIÓ D'INTERFERÈNCIA: És la suma de les puntuacions d'interferència que s'han indicat cada vegada que s'ha marcat "SÍ" en un ítem. Aquesta puntuació es calcula independentment del nombre de "SÍ" obtinguts.
>
> PUNTUACIÓ TOTAL: És la suma de tots els "SÍ" obtinguts, a més a més de les puntuacions d'interferència marcades a cada ítem on s'ha contestat "SÍ".

Aquests dos tipus de puntuacions estan relacionades amb dos nivells de severitat de símptomes obsessius-compulsius, i partir d'ambdues s'han considerat dos punts de tall: 1) Punt de tall de 25 al LOI-CV, pel que fa a la puntuació d'interferència (Berg i cols., 1988) i que ha estat utilitzat per altres autors (Brynska i Wolanczyk, 2005; Maggini i cols., 2001), 2) Punt de tall de 21 al LOI-CV, pel que fa a la puntuació total (Canals i cols., 2012b).

La versió espanyola de l'***Screen for Childhood Anxiety and Related Emotional Disorders*** (SCARED) (Birmaher i cols., 1997): qüestionari autoinformat que consta de

41 ítems per a avaluar la presència de símptomes de trastorns d'ansietat corresponents al DSM-IV. Es pot administrar a subjectes amb edats compreses entre els 8 i els 18 anys, als quals se'ls pregunta sobre la freqüència en que es presenta un determinat símptoma a partir d'una escala del 0-2: 0 (mai), 1 (a vegades), 2 (sovint). L'SCARED va mostrar una bona consistència interna (α=0,86) i està format per 4 factors anomenats: **somatització/pànic** (12 ítems; α=0,78), **fòbia social** (7 ítems; α=0,69), **ansietat generalitzada** (9 ítems; α=0,69) i **ansietat de separació** (13 ítems; α=0,70) (Vigil-Colet i cols., 2009). Es va trobar que a l'SCARED el punt de tall òptim era el de 25, en primer lloc perquè era el mateix que havia proposat l'autor del qüestionari a partir d'un estudi amb mostra clínica (Birmaher i cols., 1999), i en segon lloc, per la seva alta sensibilitat i especificitat per a la detecció de nens amb ansietat, en una mostra comunitària (Canals i cols., 2012a).

La versió espanyola del ***Children's Depression Inventory*** (CDI) (Kovacs, 1992): qüestionari autoinformat que es pot administrar a subjectes amb edats compreses entre els 7 i els 17 anys. Està format per 27 ítems, els quals serveixen per a avaluar la presència de símptomes depressius. El subjecte selecciona la frase de cada grup que millor descriu com s'ha sentit en les dues setmanes prèvies. El CDI en versió espanyola ha mostrat tenir una bona consistència interna en mostres clíniques i en mostres comunitàries (entre α=0,81 i α=0,85) (Figueras i cols., 2010). Una puntuació de 17 va ser considerada el punt de tall de risc de depressió (Canals i cols., 1995) .

La versió espanyola del ***Child Symptom Inventory-4*** (CSI-4) (Gadow i Sprafkin, 1998): instrument de cribratge basat en criteris del DSM-IV. La versió per a pares conté 97 ítems amb un format de resposta de 4 punts. Existeixen dos procediments per a puntuar: recompte de símptomes (categorial) i severitat dels símptomes (dimensional). Per a la correcció categorial, un símptoma específic és considerat clínicament rellevant si és puntuat com a que es produeix sovint o molt sovint, mentre que la correcció dimensional és simplement la suma de les puntuacions als ítems per a una categoria de símptomes particular. El CSI-4 ha demostrat ser un instrument vàlid, i la versió espanyola té una bona consistència interna (α=0,99) (Angulo i cols., 2010).

La ***Mini-International Neuropsychiatric Interview for Kids*** (M.I.N.I.-Kid) (Sheehan i cols., 1998): entrevista diagnòstica estructurada per administrar a nens d'entre 6 i 17 anys, està basada en criteris diagnòstics del DSM-IV i ICD-10. És un instrument curt i acurat que serveix per a diagnosticar fins a 23 trastorns de l'eix I. El temps d'administració és d'aproximadament uns 30 minuts.

La versió espanyola del ***Youth's Inventory-4*** (YI-4) (Gadow i Sprafkin, 1999): instrument autoinformat que està format per 120 ítems que serveixen per a avaluar símptomes emocionals i conductuals del DSM-IV a joves d'entre 12 i 18 anys. Les respostes del YI-4 poden proporcionar una valuosa informació sobre com percep els seus problemes el propi subjecte. La consistència interna que el YI-4 ha demostrat amb les nostres dades és satisfactòria (α=0,95).

## 4.4. Procediment

Abans d'iniciar l'estudi aquest projecte va ser aprovat pel Comitè Ètic de la Universitat Rovira i Virgili per a la investigació amb persones. També es va obtenir el permís corresponent del Ministeri d'Educació del Govern de la Generalitat de Catalunya.

Una mostra representativa de subjectes procedents de 13 escoles públiques i concertades de la ciutat de Reus, van ser seleccionada d'entre 26 escoles que pertanyien a 5 àrees representatives de la ciutat. Després es va contactar amb els directors dels 13 centres, obtenint la conformitat de tots ells per a la realització de l'estudi a la seva escola. Posteriorment es va enviar una carta a tots els pares per a informar-los de l'estudi i adjuntant-los-hi el consentiment informat en cas que acceptessin la participació del seu fill/a.

> **Primera fase:** Va tenir lloc durant el curs acadèmic 2006/2007. En aquesta primera fase els subjectes es trobaven cursant quart, cinquè i sisè de primària. Els participants van ser sotmesos a un cribratge a través de les seves respostes a qüestionaris d'ansietat, depressió i de símptomes obsessius-compulsius (SCARED, CDI, i LOI-CV). També es van recollir dades sociodemogràfiques i antropomètriques.

**Segona fase:** Va tenir lloc en el transcurs del curs acadèmic 2007/2008. Es va seleccionar una submostra formada per un grup de subjectes que havien obtingut puntuacions de risc als qüestionaris administrats a la primera fase i un altre grup format per subjectes control, que no havien obtingut puntuacions de risc però que presentaven les mateixes característiques quant a gènere, edat i escola. Es va realitzar un re-test amb els qüestionaris de la primera fase i també es van realitzar diagnòstics psicopatològics mitjançant l'ús de l'entrevista estructurada M.I.N.I.-Kid. Es va avaluar també el rendiment acadèmic dels subjectes participants i els pares van respondre el CSI-4.

**Tercera fase:** Va ser conduïda durant el curs acadèmic 2009/2010 (tres anys després de l'inici de l'estudi) convidant a participar-hi a tots els subjectes de la segona fase. Durant la tercera fase de seguiment es va realitzar un re-test amb els qüestionaris SCARED i LOI-CV, es van administrar els qüestionaris de símptomess YI-4 i CSI-4, i es van recollir dades sobre el rendiment acadèmic dels participants, sobre la qualitat de les seves relacions socials, i sobre la possible presència d'esdeveniments vitals estressants. També es van obtenir dades sociodemogràfiques, antropomètriques i genètiques.

Els participants van anar completant les proves en petits grups d'entre tres o quatre persones, i els investigadors encarregats de la recerca van ser-hi presents tota l'estona amb l'objectiu de donar les instruccions corresponents als nens, i resolent qualsevol dubte que es produís.

## 4.5. Variables estudiades

Les principals variables estudiades es representen a continuació de manera esquemàtica (veure la Figura 3).

| | FASE 1 | FASE 2 | FASE 3 |
|---|---|---|---|
| ANSIETAT | SCARED | SCARED<br>MINI-Kid | SCARED<br>YI-4<br>CSI-4 (pares) |
| TOC | LOI-CV | LOI-CV<br>MINI-Kid | LOI-CV<br>YI-4<br>CSI-4 (pares) |
| DEPRESSIÓ | CDI | CDI<br>MINI-Kid | YI-4<br>CSI-4 (pares) |

**Figura 3.** Esquema de les principals variables estudiades

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# 5.Resultats

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# 5. Resultats

## 5.1. Factors de risc sociodemogràfics i/o psicopatològics del diagnòstic de TOC


**Socio-demographic and psychopathological risk factors in obsessive-compulsive disorder: Epidemiologic study of school population**

Núria Voltas, Carmen Hernández-Martínez, Victoria Arija, Josefa Canals

**INFORMACIÓ REVISTA:**

*International Journal of Clinical and Health Psychology*

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**Resum:** Els resultats obtinguts mostren que els factors de risc de TOC clínic són símptomes relacionats amb l'ansietat com ara les manifestacions somàtiques o l'ansietat de separació. En canvi, els factors de risc de TOC subclínic són els símptomes més aviat de tipus obsessiu, com les preocupacions obsessives. No es troba una relació significativa entre els factors sociodemogràfics i el TOC, encara que a través del model multivariant de regressió logística es pot observar una relació amb el nivell socioeconòmic. S'observa que un menor nivell socioeconòmic és un factor de risc de TOC clínic.

A nivell transversal, el TOC clínic és explicat per la simptomatologia d'ordre, comprovació i neteja, la qual pot ser considerada de major severitat dins dels símptomes que formen part del TOC. D'altra banda persisteix la relació entre el TOC subclínic i les preocupacions obsessives, alhora que s'hi afegeixen les supersticions i les compulsions mentals i el TDAH de tipus hiperactiu-impulsiu informat pels pares.

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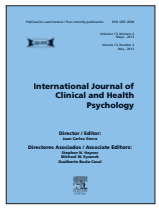

ORIGINAL ARTICLE

# Socio-demographic and psychopathological risk factors in obsessive-compulsive disorder: Epidemiologic study of school population

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**KEYWORDS**
Risk factors;
Obsessive-compulsive disorder;
Children;
Survey descriptive study

**Abstract** We assessed the presence of emotional disorders (obsessive-compulsive, anxiety and depressive) in 1,514 Spanish non-referred children (8-12 years old) to investigate the predictive ability of psychopathological and socio-demographic characteristics, and identify which of these were possible correlates for clinical obsessive-compulsive disorder (OCD) and subclinical OCD. At one year later, 562 subjects (risk group and without risk group) were re-assessed and we established the OCD diagnoses or the subclinical OCD diagnoses. We found that 20 participants presented clinical OCD and 46 participants presented subclinical OCD. Somatic and separation anxiety symptomatology were good predictors for clinical OCD, and obsessive concern was a predictor for subclinical OCD. Clinical OCD was associated with order/checking/pollution symptoms and with a lower socioeconomic status (SES). Subclinical OCD was associated with hyperactive and impulsive manifestations, obsessive concern, and superstition/mental compulsion. An early detection and the follow-up of anxiety or obsessive symptoms in children may be important for preventing the course of OCD.


**PALABRAS CLAVE**
Factores de riesgo;
Trastorno obsesivo-compulsivo;
Niños;
Estudio descriptivo por encuesta

**Resumen** Con el objetivo de investigar la capacidad predictiva de características psicopatológicas y sociodemográficas sobre el diagnóstico del trastorno obsesivo compulsivo (TOC) clínico y subclínico, y observar las posibles asociaciones entre estas variables y los dos tipos de diagnósticos, 1.514 escolares españoles con edades comprendidas entre 8 y 12 años completaron cuestionarios de riesgo de trastornos emocionales (obsesivo-compulsivos, de ansiedad y de depresión). Al año siguiente, 562 sujetos (grupo de riesgo y grupo sin riesgo) fueron re-evaluados realizándose el diagnóstico de TOC o de TOC subclínico. De ellos, 20 sujetos presentaron TOC clínico y 46 presentaron TOC subclínico. La ansiedad de separación y los síntomas somáticos

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resultaron ser buenos predictores para el diagnóstico de TOC clínico, mientras que la preocupación obsesiva fue un predictor significativo para el TOC subclínico. El TOC clínico está asociado a un nivel socioeconómico bajo y a síntomas de orden/comprobación/contaminación y el TOC subclínico se relaciona significativamente con manifestaciones de hiperactividad e impulsividad, preocupaciones obsesivas, supersticiones y compulsiones mentales. La detección precoz y el seguimiento de los síntomas ansiosos y de obsesividad en los niños pueden ser muy importantes para la prevención de trastornos como el TOC.


Obsessive-compulsive disorder (OCD) is considered one of the most common serious mental illnesses (Heyman, Mataix-Cols, & Fineberg, 2006). According to some authors, it is indisputable that a significant number of individuals in the community suffer from OCD (Eisen et al., 2010; Stewart et al., 2004) and that they are at risk of experiencing other psychiatric conditions (Marcks, Weisberg, Dyck, & Keller, 2011). In addition, Micali et al. (2010) state that paediatric OCD can be a chronic condition that persists into adulthood, so early recognition and treatment might prevent chronicity. According to Stewart et al. (2004), OCD is now being reported to be more prevalent in the paediatric population than previously, when it was considered rare, and it is increasingly becoming the focus of interest in child and adolescent psychiatry because it is a condition with important implications for social functioning, school and family and quality of life (Eisen et al., 2006; Lochner et al., 2003). Several epidemiological studies in community samples of children and adolescents have reported prevalence ranging from 0.1% to 4% (Douglass, Moffitt, Dar, McGee, & Silva, 1995; Heyman et al., 2001; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993) and in a recent study conducted in a Spanish community sample we found an estimated prevalence of OCD of 1.8% (Canals, Hernández-Martínez, Cosi, & Voltas, 2012).

Although plenty is known about how to treat OCD (Olatunji, Davis, Powers, & Smits, 2013; Rosa-Alcázar, Sánchez-Meca, Gómez-Conesa, & Marín-Martínez, 2008), there is little data regarding the risk factors that precede OCD. This disorder has a complex aetiology involving both genetic and environmental factors; the genetic causes of OCD are largely unknown despite the identification of several promising candidate genes and linkage regions (Mathews et al., 2012). In relation to the environmental factors, Grisham et al. (2011) have associated adverse prenatal, perinatal or postnatal experiences with an increased risk of developing obsessive-compulsive (OC) symptoms in adulthood. Also those authors found that a more difficult temperament in early childhood was associated with OCD. In other terms, the OCD may be caused by an autoimmune response to streptococcal infections (Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections, PANDAS) (Swedo et al., 1998).

In terms of socio-demographic factors, being male seems to be a risk factor in early onset cases (Walitza, Melfsen, Jans, & Zellmann, 2011) and although it has been poorly studied in children and adolescents, lower socioeconomic status (SES) has also been related to OCD (Heyman et al., 2001). In adults economic impairment and unemployment have been related to OCD (Grabe et al., 2000; Himle et al., 2008). Academic performance has also been related to OCD although the findings are still mixed as yet. Whereas Himle et al. (2008) found that adults with OCD had lower educational success because their academic performance began to suffer when they were children; others such as Degonda, Wyss, and Angst (1993) found that subjects with OC symptoms differed from controls by exhibiting higher educational levels.

Furthermore, as we have mentioned, the relationships between OCD and other psychiatric conditions are highly prevalent among children and adolescents. In this regard, we have found high rates of comorbidity for OCD in Canals, Hernández-Martínez, Cosi, and Voltas (2012), particularly in relation to anxiety and depression disorders. De Mathis et al. (2012) studied the impact of the first manifested psychiatric diagnosis on the clinical development of OCD using adult OCD patients. They found that participants who reported antecedent symptoms of separation anxiety were shown to develop further additional anxiety and somatoform disorders such as somatization and more severe current depressive symptoms. Likewise they found that patients presented a worsening course of OCD if they had first been diagnosed with attention deficit hyperactivity disorder (ADHD). In fact it is known that ADHD symptoms in adolescence predicted more OCD symptoms in early adulthood (Peterson, Pine, Cohen, & Brook, 2001).

Other authors found a relationship between OCD and eating disorders (Kim, Ebesutani, Wall, & Olatunji, 2012), particularly those disorders that present high body mass index (BMI), such as binge-eating disorder (Claes, Nederkoorn, Vandereycken, Guerrieri, & Vertommen, 2006). Some studies have demonstrated relationships between appetite regulating peptides and OC symptoms (Hillemacher et al., 2007), so it is difficult to know if having high BMI may be a cause or consequence of the OCD and eating disorders.

Recently, Taylor (2011) confirmed that OC symptomatology has a complex etiological architecture, which does not appear to be adequately captured yet, and so our purpose was to identify factors that could contribute to the early development of this disorder or to ascertain which variables could be related to OCD regardless of the genetic or other type of biological risk factors, because this is essential for the development of prevention and treatment programs. For this reason, our main aim was to carry out a follow-up epidemiological study to observe the predictive ability of psychopathological and socio-demographic characteristics and possible correlates for two levels of severity of OCD: clinical OCD and subclinical OCD.

## Method

### Participants

2,023 children were invited to participate in a follow-up study of emotional disorders. The children came from 13 primary schools in Reus (Catalonia, Spain) randomly chosen from the towns' state schools and state-subsidized private schools. The study began in 2007 and 1,514 children with a mean age of 10.23 (*SD* = 1.23) agreed to participate (720 boys and 794 girls). Of these 1,514 subjects, a total of 39.5% belonged to families with low SES, 42.5% to families of medium SES and 18% to families of high SES. 87.5% of the sample was born in Spain, and 85.9% belonged to a nuclear family. One year later, in the second stage, 562 subjects (254 boys and 308 girls) between 9 and 13 years of age (*M* = 11.25; *SD* = 1.04) were selected either as subjects at risk of emotional disorders (41.8%) or as belonging to a control group with no risk (58.2%). The attrition of the risk subjects from the 1st to the 2nd phase was 16%. If a control subject was invited to participate in the 2nd phase and declined, we selected another participant with similar characteristics from the 1st phase.

### Instruments

- Leyton Obsessional Inventory-Child Version Survey (LOI-CV; Berg, Whitaker, Davies, Flament, & Rapoport, 1988) is a self-report of a 20-item questionnaire that aims to determine the presence or absence (using in the item *Yes/No*) of a number of obsessive preoccupations and behaviours, and that includes a rating of interference with personal functioning for each positive response (range 0-3, no interference-interferes a lot). The internal consistency of the Spanish version is good (Cronbach's α = .90) and is composed of three factors called *Order/checking/pollution* (7 items; Cronbach's α = .82), *Obsessive concern* (7 items¸ Cronbach's α = .81) and *Superstition/mental compulsion* (6 items; Cronbach's α = .77). This questionnaire has been proven to be a valid screening instrument for assessing OCD or OC symptoms in children and adolescents (Canals, Hernández-Martínez, Cosi, Lázaro, & Toro, 2012).
- Screen for Childhood Anxiety and Related Emotional Disorders (SCARED; Birmaher et al., 1997). The SCARED is a self-report questionnaire that assesses DSM-IV anxiety disorder symptoms in children and adolescents from 8 to 18 years old. It consists of 41 items, and children are asked the frequency of each symptom on a 3-point-scale: 0 (*almost never*), 1 (*sometimes*), 2 (*often*). The internal consistency of the Spanish version is good (Cronbach's α = .86) and is composed of 4 factors called *Somatic/panic* (12 items; Cronbach's α = .78), *Social phobia* (7 items; Cronbach's α = .69), *Generalized anxiety* (9 items; Cronbach's α = .69), and *Separation anxiety* (13 items, Cronbach's α = .70) (Vigil-Colet et al., 2009).
- Children's Depression Inventory (CDI; Kovacs, 1992) is a 27-item, self-report, symptom-oriented scale suitable for young people aged 7 to 17. The CDI is sensitive to changes in depressive symptoms over time, and is a useful index of the severity of the depressive syndrome. The Spanish version has demonstrated good internal consistency in community and clinical samples (Cronbach's α = .81 to Cronbach's α = .85) (Figueras, Amador-Campos, Gómez-Benito, & Del Barrio, 2010).
- Child Symptom Inventory (CSI-4; Gadow & Sprafkin, 1998) is a screening instrument based on DSM-IV criteria. The parent version used in this study contains 97 items with a 4-point response format. There are two scoring procedures: symptom count (categorical) and symptom severity (dimensional). For the categorical correction, a specific symptom is considered to be a clinically relevant problem if it is rated as occurring often or very often, whereas the dimensional correction is simply the sum of the item scores for a particular symptom category. The CSI-4 has been demonstrated to be valid (Sprafkin, Gadow, Salisbury, Schneider, & Loney, 2002) and the Spanish version of CSI-4 has shown excellent internal consistency (Cronbach's α = .99) (Angulo et al., 2010).
- Mini-International Neuropsychiatric Interview for Kids (MINI-Kid; Sheehan et al., 1998) is a structured diagnostic interview for children from 6 to 17 years old based on DSM-IV and ICD-10 psychiatric disorders. It is a short and accurate instrument for diagnosing 23 axis I disorders. Interrater and test-retest Kappa were substantial to almost perfect (.64–1) for all individual MINI-Kid disorders except dysthymia. For OCD the interrater test kappa was .94 and the retest Kappa was .75. The interview takes approximately 30 minutes to administer. The reliability and validity of MINI-Kid has recently been demonstrated (Sheehan et al., 2010). OCD were assessed as well as depressive, bipolar, anxiety, tic, psychotic, eating and adjustment disorders and disruptive (ADHD, and conduct) disorders. The OCD diagnostic agreement (Kappa index) between the MINI-Kid and the LOI-CV was .45.
- Anthropometry, weight and height were evaluated and we obtained the BMI.
- In order to assess the socio-demographic characteristics of the sample, a socio-demographic questionnaire designed for this study was used. The children answered questions about age, gender, place and date of birth, family type, occupation of parents and other subjects. To assess academic performance, teachers were asked by one question about the children's academic performance with three response options: below average, average or above average. SES was determined using the Hollingshead

index (Hollingshead, 2011). This index allows the social status of each individual to be determined by categorizing his or her occupation into one of nine categories (from unskilled work to highly skilled work) and his or her level of education into one of seven categories (from non-completed primary education to completed higher education). The status score is estimated by multiplying the occupation scale value by a weight of five and the education scale value by a weight of three and then combining the two scores. For this study, we determined family SES by combining the data obtained from the father and the mother. The scores range from 0 to 66, therefore, to obtain three categories (low, medium and high) we considered scores lower than 22 to be low SES, scores between 23 and 44 to be medium, and scores over 44 to be high.

### Procedure

Before beginning the study, permission from the Department of Education of the Catalan Government was obtained. Then we selected a representative sample of subjects. Cluster sampling was conducted by randomly selecting a set of 13 schools (7 state schools and 6 state-subsidized private schools) from a total of 26 schools and from all five representative areas of Reus, Spain (a medium-sized town of 100,000 inhabitants). We then contacted the 13 school boards, all of whom agreed to participate. After that, we sent all parents a letter to inform them about the study and to ask for their written informed consent. A two-phase epidemiological study design was used. In the 1st phase we assessed the anxiety symptoms (SCARED), depressive symptoms (CDI), OC symptoms (LOI-CV), and the socio-demographic data of 1,514 subjects. This data was collected using a questionnaire designed for this study in which we asked children about their parents' jobs, family structure and other socio-demographic variables. Over the following academic year, the 2nd phase was conducted. A subsample of subjects at high risk of emotional and obsessive-compulsive disorders and a subsample of control subjects at low risk paired by age, gender and school were selected. High risk status was determined when the subject in the 1st phase obtained a high score in the SCARED and/or in the CDI and/or in the LOI-CV. In this second stage, the MINI-Kid was administered and the SCARED, the CDI and the LOI-CV were re-administered. The interviews were administered to the children on the same day or during the week after the questionnaires were completed and the interviewers were blind to the test results. To obtain diagnoses, data from a psychopathological test completed by the students' parents (CSI-4) were taken into account, and when researchers had questions, parents were telephoned to obtain more information. When the child met the full criteria for OCD diagnosis according to the DSM-IV, clinical OCD was assigned, and when the child met all criteria for OCD diagnosis except the criteria of interference, subclinical OCD was assigned. So, 20 subjects presented OCD diagnosis, and 46 subjects presented subclinical OCD diagnosis. The parents of children, who were diagnosed with any disorder, were notified about it by telephone.

The participants completed the questionnaires in groups of three or four subjects. Professional child psychologists gave the children instructions on how to answer the surveys and helped them during the session. The MINI-Kid was individually administered by these same child psychologists, who had been trained to administer the interview until they agreed on the diagnoses in 90% of the cases.

### Data analysis

To examine the risk factors, stepwise logistic regression models were used. Before performing the regression models, collinearity between the variables were assessed by computing Pearson correlations between the candidate variables to enter in the model. The LOI-CV total score was collinear with LOI-CV factors, and the SCARED total score was also collinear with the SCARED factors, so the SCARED and LOI-CV factors were selected instead of the total scores. The correlation between the SCARED and the LOI-CV factors for the 1st and 2nd phases were below .5 and were therefore not considered collinear.

The regression models were performed in two steps. In the first step the socio-demographic, anthropometric and psychopathological variables collected in the 1st phase (LOI-CV factor scores, SCARED factor scores, CDI total score, BMI, SES, age, gender, family type, and birth place) were considered, and in the second step the academic performance and all the psychopathological variables collected in the 2nd phase (LOI-CV factor scores, SCARED factor scores, CDI total score, CSI-4 scores related to Disruptive Behavior Disorders such as Attention Deficit Hyperactivity Disorder-Inattentive (ADHD-I), Attention Deficit Hyperactivity Disorders-Hyperactive-Impulsive (ADHD-HI), Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), and Generalized Developmental Disorder (GDD) were added to the first step variables.

The Bonferroni correction was applied to control the increase in type I error caused by multiple comparisons, which meant that the level of significance used was .01. The data were analyzed using the SPSS 19.0.

## Results

Logistic regression models were conducted to examine whether socio-demographic and psychopathological factors predicted clinical OCD or subclinical OCD diagnoses. As regards the clinical OCD diagnosis (see Table 1), we used the psychopathological, the socio-demographical and the anthropometrical data collected in the 1st phase to step 1, and we observed that somatic/panic and separation anxiety factors of the SCARED were good predictors. Step 1 explained 20.3% of the OCD diagnoses. We added the psychopathological data (emotional data from the child and behavioural data from the parents) and the academic performance obtained in the 2nd phase to step 2, which accounted for 63.9%, and we found that the best related factors were the SES, the somatic/panic factor of the SCARED administered in the 1st phase, and the score in the order/checking/pollution factor of the LOI-CV administered in the 2nd phase.

**Table 1** Logistic regression models to predict clinical obsessive-compulsive disorder diagnosis.

| **Clinical OCD diagnosis (*n* = 20) vs. non-clinical OCD diagnosis (*n* = 542)** | | | |
|---|---|---|---|
| | **B** | **Odds ratio (95% CI)** | ***p*** |
| *Step 1* | | | |
| 1st phase SCARED somatic/panic | .138 | 1.148 (1.020-1.293) | .018 |
| 1st phase SCARED separation anxiety | .173 | 1.189 (1.032-1.370) | .011 |
| | $R^2$ Negelkerke * 100 = 20.3 | | |
| | Chi-square$_{2.510}$ = 26.991 | | |
| | *p* = .001 | | |
| *Step 2* | | | |
| SES | .720 | .488 (.263-.900) | .003 |
| 1st phase SCARED somatic/panic | .222 | 1.248 (1.053-1.480) | .002 |
| 2nd phase LOI-CV order/checking/pollution | .553 | 1.738 (1.355-2.230) | .001 |
| | $R^2$ Negelkerke * 100= 63.9 | | |
| | Chi-square$_{3.300}$ = 55.272 | | |
| | *p* = .001 | | |

95% CI, 95% confidence interval; LOI-CV, Leyton Obsessional Inventory-Child Version Survey; OCD, obsessive-compulsive disorder; SCARED, Screen for Childhood Anxiety and Related Emotional Disorders; SES, socioeconomic status.
Candidate variables to enter in step 1: 1st phase LOI-CV factor scores→ order/checking/pollution; obsessive concern and superstition/mental compulsion, age (years), SES (total score), BMI (total score), 1st phase CDI (total score), 1st phase SCARED factor scores→ somatic/panic; social phobia; generalized anxiety and separation anxiety; gender (1: boy; 2: girl), family type (0: single-parent; 1: nuclear), birth place (0: foreign; 1: native).
Candidate variables to enter in step 2: To the variables in step 1, we added academic performance (1: high; 2: low); 2nd phase LOI-CV factor scores→ order/checking/pollution; obsessive concern and superstition/mental compulsion; 2nd phase CDI (total score); 2nd phase SCARED factor scores→ somatic/panic; social phobia; generalized anxiety and separation anxiety and CSI-4 scores (ADHD-I, ADHD-HI, ODD, CD, GDD).

**Table 2** Logistic regression models to predict subclinical obsessive-compulsive disorder diagnosis.

| **Subclinical OCD diagnosis (*n* = 46) vs. non OCD-manifestations (*n* = 496)** | | | |
|---|---|---|---|
| | **B** | **Odds ratio (95% CI)** | ***p*** |
| *Step 1* | | | |
| 1st phase LOI-CV obsessive concern | .097 | 1.101 (1.035-1.173) | .002 |
| | $R^2$ Negelkerke * 100 = 4.5 | | |
| | Chi-square$_{1.493}$ = 9.197 | | |
| | *p* = .002 | | |
| *Step 2* | | | |
| 2nd phase LOI-CV obsessive concern | .118 | 1.125 (1.011-1.252) | .013 |
| 2nd phase LOI-CV superstition/mental compulsion | .247 | 1.280 (1.115-1.470) | .001 |
| 2nd phase CSI-4 ADHD-HI | .118 | 1.125 (1.039-1.218) | .004 |
| | $R^2$ Negelkerke * 100= 29.6 | | |
| | Chi-square$_{2.289}$ = 39.816 | | |
| | *p* = .001 | | |

95% CI, 95% confidence interval; ADHD-HI, Attention Deficit Hyperactivity Disorders-Hyperactive-Impulsive; LOI-CV, Leyton Obsessional Inventory-Child Version Survey; OCD, obsessive-compulsive disorder.
Candidate variables to enter in step 1: 1st phase LOI-CV factor scores→ order/checking/pollution; obsessive concern and superstition/mental compulsion, age (years), SES (total score), BMI (total score), 1st phase CDI (total score), 1st phase SCARED factor scores→ somatic/panic; social phobia; generalized anxiety and separation anxiety; gender (1: boy; 2: girl), family type (0: single-parent; 1: nuclear), birth place (0: foreign; 1: native).
Candidate variables to enter in step 2: To the variables in step 1, we added academic performance (1: high; 2: low); 2nd phase LOI-CV factor scores→ order/checking/pollution; obsessive concern and superstition/mental compulsion; 2nd phase CDI (total score); 2nd phase SCARED factor scores→ somatic/panic; social phobia; generalized anxiety and separation anxiety and CSI-4 scores (ADHD-I, ADHD-HI, ODD, CD, GDD)

When we performed the logistic regression models for the subclinical OCD diagnosis (see Table 2), we found that the model explained 4.5% of the subclinical OCD and that the best predictor in step 1 was the obsessive concern factor of the LOI-CV. When we introduced the 2nd phase variables (step 2), the obsessive concern and the superstition/mental compulsion factors of the LOI-CV administered in the 2nd phase were significantly related to the subclinical OCD and, moreover, we could observed that the ADHD-HI score was a significant correlate with the subclinical OCD. The explained variance increased to 29.6%.

## Discussion

The objective of this study was to examine the possible ability of psychopathological and socio-demographic characteristics to predict the subsequent diagnosis of early childhood clinical OCD or subclinical OCD, and there have been few studies in this area and very few that have used children from community samples. Moreover we wanted to observe the possible relation between some of these characteristics and the two types of diagnoses. These results provide important evidence that has clinical implications; the risk factors associated with subclinical OCD, either as predictors or related factors, are obsessive symptoms such as obsessive concern or superstition, whereas factors that could predict or that were related to clinical OCD were anxiety symptoms. Therefore, we suggest that subclinical OCD children present a pattern of obsessiveness and subjects with a more severe OCD diagnosis have previously present a pattern of anxiety symptoms. We also believe that it is interesting to take into account the less severe form of OCD because it could be a possible indicator of long term clinical OCD. Alternatively, the subjects could present subclinical OCD symptoms during the prospective period because full remission is rare, which is consistent with the view of OCD as a chronic and persistent disorder (Eisen et al., 2010).

In agreement with the results showed in this study, Brynska and Wolanczyk (2005) found more obsessive symptoms in the subclinical OCD group than compulsive symptoms. The most common obsessions were a fear of saying certain things, which can be linked to the obsessive concern factor, and obsessive symptomatology, such as magical thoughts or lucky/unlucky numbers, which are symptoms that can be related to the superstition/mental compulsion factor. On the other hand, we know that order/checking/pollution as a manifestation of OC is more severe, and this may be the reason why this type of symptom was more highly related to clinical rather than subclinical OCD in our study. These results also support those of Brynska and Wolanczyk (2005), who found in subjects with clinical OCD that the most frequent compulsions were checking, ordering and washing and cleaning. In addition, our results have shown that some anxious symptoms such as somatic/panic and separation anxiety could be positive predictors of clinical OCD. These data are consistent with those found in adults by Cath, Van Grootheest, Willemsen, Van Oppen, and Boomsma (2008), which supported the hypothesis that somatic was one of the major complaints and which showed the highest scale scores for somatic complaints in concordant high monozygotic pairs of twins with OC symptoms. Furthermore, Storch, Merlo et al.(2008) observed that somatic symptoms were highly prevalent among young people with OCD and had a significant impact on the clinical presentation of the disorder. In this regard, Zolog et al. (2011) found that somatic complaints were frequently associated with emotional problems and in our study somatic complaints are previous manifestations of OCD. On the other hand, data showing that separation anxiety symptomatology is a predictor of OCD supports the data of Ballesteros and Ulloa (2011), who found that OCD is frequently comorbid with anxiety disorders such as separation anxiety, and the data of Kossowsky, Wilhelm, Roth, and Schneider (2012), who found that separation anxiety disorder (SAD) is one of the most common anxiety disorders in childhood and is highly predictive of adult anxiety disorders. In this regard, Mroczkowski et al. (2011) stated that SAD usually has onset earlier than OCD and may influence the clinical course of OCD. Furthermore, worries that children with separation anxiety have can take on obsessional qualities and it can sometimes be difficult to distinguish between SAD and OCD. Moreover Mroczkowski et al. (2011) also concluded that this kind of anxiety could be correlated with adult emotional disorders, including panic disorder and major depression. On the other hand, the relation found in our study between OCD and the most common anxiety symptoms in children corroborate the classification of OCD as an anxiety disorder.

Although there are studies suggesting that levels of depression may be the product of OC symptoms (Storch et al., 2012), this is not reflected in our results, which means that depressive symptoms may be a more long term consequence for children who have suffered OCD. On the other hand, our results did not show any relation between OCD and age, gender, birth place or family type. The absence of any relation may indicate that socio-cultural factors do not influence OCD, as stated by Himle et al. (2008).

Regarding the remaining factors, despite the known relationship between OCD and eating problems (Kim et al., 2012) we found no significant results indicating that the high BMI was a risk factor for OCD. Our data also did not support the association between OCD and academic performance as suggested by Himle et al. (2008). However, in their sample Heyman et al. (2001) found that subjects belonging to lower socioeconomic classes presented higher rates of OCD, and this was in keeping with our results, which showed a relation between lower SES and clinical OCD. Another interesting finding of our work was the association between ADHD-HI and subclinical OCD, and this finding is comparable with that of Sheppard et al. (2010), who found that ADHD symptoms are quite prominent among OCD affected individuals. In this regard, Grisham et al. (2011) suggested that higher levels of hyperactive problems in middle childhood were associated with increased risk of some OC symptoms. Therefore we have to be careful when hyperactive and impulsive symptoms are presented together with the less severe

form of the disorder because, as Geller (2006) reported, both disorders contribute to morbid dysfunction and require independent treatment.

In conclusion, we believe that data provided by our study contributes to the understanding of paediatric OCD because we have studied a non-clinical sample whose age period has been described in the literature as the period when OCD first emerges. Another strength of our study was that we used OC symptoms and also OCD diagnoses. We aimed to use the best informant for each type of psychopathological manifestation (Comer & Kendall, 2004; Cosi, Canals, Hernández-Martínez, & Vigil-Colet, 2010) and so we used the CSI-4 to obtain information about behavioural symptoms from the parents and we obtained information about emotional symptoms from the children. However, our study does have some limitations that are worth mentioning. First, our follow-up was only one year and we believe that a longer follow-up study could be useful in this area, because as stated by Eisen et al. (2010), little is known about the long-term course of OCD. Another limitation could be the sample size, because the number of subjects with diagnoses was limited. Furthermore, although we speak of predictor factors of OCD, we do not know if the children diagnosed of OCD in the 2nd phase had had any OCD diagnosis the previous year (1st phase).

In summary, the results showed in the present study suggest that behavioural symptoms and obsessive concern indicate the development of subclinical OCD. Also, the early detection of anxiety symptoms in children is very important because it means that the appropriate treatment can be undertaken, to prevent or improve the course of anxiety disorders such as OCD.

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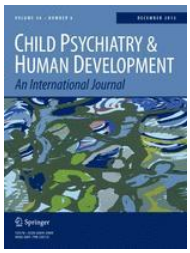
## 5.2. Estudi prospectiu de la simptomatologia obsessiva-compulsiva en una mostra comunitària d'escolars




**A prospective study of paediatric obsessive-compulsive symptomatology in a Spanish community sample**

Núria Voltas, Carmen Hernández-Martínez, Victoria Arija, Estefania Aparicio, Josefa Canals

**INFORMACIÓ REVISTA:**

*Child Psychiatry & Human Development*

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**Resum:** Els resultats mostren que les puntuacions al LOI-CV disminueixen amb el pas del temps independentment de l'edat i el sexe dels subjectes. Malgrat això, les taxes de prevalença, persistència i incidència, segons dos nivells de severitat dels símptomes obsessius-compulsius (punt de tall 21 en la puntuació total del LOI-CV i punt de tall 25 en la puntuació d'interferència del LOI-CV) oscil·len entre un 4,8% i un 30,4%, un 9,3% i un 28,4%, i un 1,1% i un 14,4% respectivament. Més d'un 30% d'escolars presenten cronicitat dels símptomes obsessius-compulsius si tenim en compte les xifres de recurrència i persistència presentades als tres anys.

L'anàlisi de regressió logística a la tercera fase, permet observar que els símptomes menys severs (punt de tall 21 al LOI-CV) estan més relacionats amb l'ansietat prèvia i amb els símptomes obsessius-compulsius previs. D'altra banda els símptomes més severs (punt de tall 25 al LOI-CV) estan més relacionats amb els símptomes depressius i també amb els símptomes obsessius-compulsius i amb els símptomes d'ansietat. El gènere no s'ha mostrat com a variable explicativa de la simptomatologia obsessiva-compulsiva.

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
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ORIGINAL ARTICLE

# A Prospective Study of Paediatric Obsessive–Compulsive Symptomatology in a Spanish Community Sample

**Núria Voltas · Carmen Hernández-Martínez · Victoria Arija · Estefania Aparicio · Josefa Canals**



**Abstract** The obsessive–compulsive manifestations course was assessed with the Leyton obsessional inventory-child version survey (LOI-CV) in a 3-year prospective study, using a non-clinical sample. From an initial sample of 1,514 school-age children who underwent symptoms screening for obsessive–compulsive, anxiety and depression, 562 subjects (risk group/without risk group) were re-assessed in the 2nd phase and 242 subjects were monitored after 3 years. LOI-CV scores significantly decreased over time independently of age and gender. The prevalence, persistence and incidence for two levels of severity of obsessive–compulsive manifestations ranged between 4.8–30.4 %, 9.3–28.4 % and 1.1–14.4 %, respectively. 34.6–64.5 % of obsessive–compulsive symptomatology was predicted by anxiety, depressive and obsessive–compulsive symptoms. For the obsessiveness (less severe form of obsessive–compulsive manifestations), the depressive symptoms were not predictors. Gender and socioeconomic status were not related with obsessive–compulsive manifestations. These data support a substantial continuity of the obsessive–compulsive manifestations and the existence of different levels of severity within the obsessive–compulsive spectrum.

**Keywords** Obsessive–compulsive symptoms · Prospective study · Non-clinical sample · School-age children

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## Introduction

It is commonly known that obsessive–compulsive disorder (OCD) in children and adolescents has been little studied in the past and may have been under-diagnosed and under-treated. OCD occurs either as the full-blown disorder, in the form of subclinical OCD or as obsessive–compulsive (OC) symptoms. In fact, several studies have used case definitions for different severity levels of the OC manifestations [1, 2]. Some epidemiological studies have demonstrated that children and adolescents often present with some form of OCD from the OCD spectrum and that it has an early age of onset [3, 4]. The prevalence of OCD from childhood to the end of adolescence ranges from 0.1 to 4 % [5–7]. Specifically, an OCD prevalence of 1.8 % was found in a Spanish non-clinical sample of school children [1]. For subclinical OCD and OC symptomatology, the rates are larger and range from 2.7 to 19 % [1, 3, 8].

Most authors regard OCD as a chronic disorder that interferes in the daily lives of the subjects and that presents high persistence rates throughout a person's life, especially if left untreated [9–11]. Eisen et al. [12] conducted a prospective clinical study in which they suggested that full remission was rare, whereas Palermo et al. [13] showed that a large frequency of children with OCD experience remission by early adulthood. Therefore, can OCD be considered a chronic condition? Are the OC symptoms in childhood evolutionary manifestations? How persistent is the disorder?

Other studies have investigated the relationship between OC symptoms and psychopathological or socio-demographic factors and data are somewhat inconsistent. As for gender, generally females reported significantly more symptoms and interference than males [3, 14]; although at early ages several authors have reported a slight male predominance [4, 15]. In this regard, Ruscio et al. [16]

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stated that nearly one quarter of boys experienced the onset of the disorder before the age of 10, whereas girls usually experienced the onset of OCD after the age of 10. Moreover, Geller [15] conducted an extensive study which compared specific OC manifestations across different age groups and found several differences between children, adolescents and adults in the frequency of particular obsessions and compulsions; children and adolescents had much higher rates of aggressive/harm obsessions than adults. Likewise, religious obsessions were over-represented in adolescents, and sexual obsessions were less frequent in children compared with adolescents and adults. In terms of compulsions, both Geller [15] and Nikolajsen et al. [11] found that only hoarding was more prevalent in children and adolescents than in adults. The results are at odds concerning the relationship between other socio-demographic variables and OC manifestations. The review by Fontenelle and Hasler [17] found that some authors observed OC symptoms in subjects had been raised in significantly higher social classes [18], whereas others such as Heyman et al. [19] reported a trend for higher rates of OCD in lower socioeconomic groups. The situation is similar for educational level. While some authors have suggested that subjects with OCD show significant impairment in their academic life [20] others have found that OCD is more common among individuals with higher educational levels [21]. In adults, Grabe et al. [22] found higher prevalence rates of OCD among subjects who were unemployed, and that subjects with OCD are less likely to be married. There is still controversy regarding the role of race-ethnicity as a predisposition factor for developing OCD; some studies have found that the black ethnic identity can have a protective role [23], whereas others have been unable to find differences in prevalence of OCD between different ethnical groups [24].

Subjects with OC manifestations are at risk of presenting higher rates of comorbidity with other psychiatric conditions [25, 26]. Thus, some authors have found that OCD and depressive disorders co-occur frequently in both adults and children [1, 27], thus suggesting that depression was a product of the OC symptoms [28]. Moreover, children with autism spectrum disorders have shown increased rates of OC manifestations [29] and conversely, paediatric OCD patients have shown increased frequencies of autism spectrum symptoms [30]. Furthermore, several authors have found higher frequencies of comorbid tic disorders, disruptive behaviour disorders and attention deficit hyperactivity disorder (ADHD) in children with OCD [27, 31]. It is important to study the possible correlates between OCD and other psychiatric conditions because the two conditions may need separate treatment, for example when OCD is presented with ADHD [15]. On the other hand, some authors have suggested that OCD with comorbid ADHD could be a specific subgroup of OCD patients whose condition follows a more homogeneous course [32].

Another issue is that sometimes shame associated with the disorder may inhibit people from disclosing the symptoms, thus delaying detection, diagnosis and treatment. Affected people are often reluctant to reveal symptoms, particularly if the symptoms are perceived as embarrassing. For this reason screening tools are needed. As other authors, we also consider that the Leyton obsessional inventory-child version (LOI-CV) [33] has important advantages in that it is brief, simple and self-reporting and, having evaluated the properties of the LOI-CV in our sample, we conclude that it is a reliable and valid instrument for detecting OCD in children from a non-clinical population [34, 35].

After reviewing the existing literature, we observed that only a few prospective studies had used community samples of early adolescents to clarify the course that OCD takes when it begins at early ages. Consequently, we decided to prospectively examine the clinical course of OC manifestations in a longitudinal epidemiological study with the main aims of: (1) exploring the relationships between the LOI-CV scores and socio-demographic variables in the 3 periods of the follow-up; (2) studying the evolution of the LOI-CV total and the factors scores throughout the follow-up, controlling for age and gender; (3) determining the course taken by the OC manifestations by estimating its prevalence, persistence, recurrence, and incidence at two levels of severity (obsessiveness and OC symptomatology); (4) exploring the predictive psychopathological factors of the two severity levels of OC manifestations at the end of the study. Taking all the above into account, we first hypothesized that, as LOI-CV scores suggest, OC manifestations vary according to gender, age and other socio-demographic characteristics. We also hypothesized that the rates of persistence and recurrence of OC are considerable, which means that it is present throughout development, and that manifestations are related to previous anxiety, depression, and OC symptoms.

## Method

### Participants

2,023 4th, 5th and 6th grade students from thirteen primary schools (7 state schools and 6 state-subsidized private schools) in Reus (a medium-sized Spanish town of 100,000 habitants) were invited to participate in an epidemiological study of anxiety and depression disorders. The study was conducted in three-phases. 1,514 students participated in the 1st phase (720 boys and 794 girls) between 8 and

12 years of age (mean = 10.23; SD = 1.23). A total of 39.5 % of the children belonged to families of a low socioeconomic status (SES), 42.5 % to families of medium SES and 18 % to families of high SES. 87.5 % of the sample was born in Spain, and 85.9 % belonged to a nuclear family. Once we had screened the 1st phase, 562 students (254 boys and 308 girls) of mean age 11.25 (SD = 1.04) were selected to participate in the 2nd phase as subjects at risk of OCD (41.8 %) or as members of a control group without risk (58.2 %). There were no significant differences between risk and control group subjects for gender ($\chi^2 = .132$, $p = .716$), birthplace ($\chi^2 = .075$, $p = .784$), family type ($\chi^2 = .227$, $p = .634$), SES ($\chi^2 = 1.306$, $p = .520$) and age ($t = .947$, $p = .344$). Two years later all 562 subjects were invited to participate in the 3rd phase follow-up and 242 subjects (95 boys and 147 girls) (mean age was 13.52, SD = .94) participated. There were no emotional and socio-demographic differences between subjects who participated in the 3rd phase and subjects who dropped out in this last step of the study. However there were differences related to the SES factor: low SES participants were associated with higher dropout rates than were medium or high SES participants ($\chi^2_{2.561} = 13.557$; $p = .001$).

## Instruments

*Leyton obsessional inventory-child version survey* (LOI-CV) [33] is a self-reported 20-item questionnaire asking about the presence or absence (described in the item Yes/No) of a number of obsessive preoccupations and behaviours, including, for each positive response, a rating of interference with personal functioning (range 0–3, no interference-interferes a lot). LOI-CV has been proven to be a valid screening instrument for assessing OCD or OC symptoms in children and adolescents [34]. Despite the fact that over the years several questionnaires have been published for assessing OC symptoms in children, some of which derive from adult assessment instruments [36–38], we nevertheless chose the LOI-CV because, when we began the present study, the LOI-CV was the most widely used instrument in Spanish clinical samples and in any case no other questionnaires for screening OC symptoms had been adapted for use in Spain. We found that the best factorial structure was a model using three factors; these three factors explained 46.30 % of the variance. The factors were the following: order/checking/pollution, obsessive concern, and superstition/mental compulsion (30.15, 8.53 and 7.62 % of the variance, respectively). Total reliability was good ($\alpha = .78$) [34]. In this study, we considered two types of LOI-CV scores: the interference score, which is the sum of the interferences regardless of the "yes" responses; and the total score, which is the sum of the "yes" score plus the interference scores. We also established two levels of severity for OC manifestations: (1) we defined an interference score of 25 or above as indicative of OC symptomatology, a cut-off point that was proposed by the author of the questionnaire [33] and that has been used by other authors [3, 14]; (2) on the basis of data obtained by Canals et al. [34] we used the total score of 21 as the cut-off point to define a less severe category for the OC manifestations, and we called this obsessiveness.

*Youth's inventory-4* (YI-4) [39] is a self-report rating scale of 120 items that evaluates DSM-IV symptoms of emotional and behaviour disorders in youths between 12–18 years old. To obtain our results we took into account nine symptom categories from this instrument, corresponding to nine types of disorders: ADHD, conduct disorders, tic disorders, eating disorders, depression, bipolar disorder, schizophrenia, schizoid personality, and substance use. The YI-4 demonstrated satisfactory internal consistency ($\alpha = .95$).

*Screen for childhood anxiety and related emotional disorders* (SCARED) [40] is a self-report questionnaire that assesses anxiety disorder symptoms in children and adolescents from 8 to 18 years old. The scale is composed of 41 items and children were asked the frequency of each symptom on a 3-point-scale: 0 (almost never), 1 (sometimes), 2 (often). The internal consistency of the Spanish version was good ($\alpha = .86$) [41]. A score of 32 was considered to be the cut-off point for risk of anxiety. Given that in Spain the cut-off has not been validated, this score corresponded to percentile 75 of our sample, the same percentile used by Birmaher et al. [42] in a sample of outpatients from the USA.

*Children's depression inventory* (CDI) [43] is a 27-item self-report symptom-oriented scale suitable for youths aged 7–17. The CDI is sensitive to changes in depressive symptoms over time and is a useful index of the severity of the depressive syndrome. The Spanish version demonstrated good internal consistency in community and clinical samples ($\alpha = .81$–$.85$) [44]. A score of 17 was considered as the cut-off point for risk of depression [45].

*Socio-demographic characteristics* of the sample were collected at baseline with a questionnaire designed for this study by the authors. The children answered questions about age, gender, place and date of birth, family type and occupation of parents. This information was corroborated by the parents. The SES was established by the Hollingshead index [46]. This index allows the social status of each individual to be determined by categorizing his or her occupation into one of nine categories (from unskilled work to highly skilled work) and his or her level of education into one of seven categories (from non-completed primary education to completed higher education). The status score is estimated by multiplying the occupation scale value by a

weight of five and the education scale value by a weight of three and then combining the two scores. We thus determined family SES on a scale from 0 to 66. This gave us three categories (low, medium and high) we considered scores lower than 22 to be low SES, scores between 23 and 44 to be medium, and over 44 to be high.

*Academic performance* was assessed by a questionnaire designed for this study by the authors. It was answered by teachers at the 2nd phase and by parents at the 3rd phase.

## Procedure

This is a prospective longitudinal study with three phases. Following approval from the *Department of Education of the Catalan Government*, we selected a representative sample of subjects. Cluster sampling was conducted by randomly selecting a set of 13 schools (7 state schools and 6 state-subsidized private schools) from a total of 26 schools from all five representative areas of Reus (Spain). We then contacted the 13 school boards, all of whom agreed to participate. After that, we sent all parents a letter to inform them about the study and to ask for their written informed consent. The 1st phase took place during the 2006/2007 academic year with a representative sample of school-age subjects (subjects in 4th, 5th and 6th primary grades). The 2nd phase (2007/2008 academic year) took place during the following academic year and the 3rd during the 2009/2010 academic year. Participants in the 1st phase were administered screening tests for anxiety symptoms (SCARED), depressive symptoms (CDI) and obsessive–compulsive disorder symptoms (LOI-CV) and were assessed on the basis of their socio-demographic data. This data was collected using a questionnaire designed for this study in which children were asked about their parents' jobs, family structure and other socio-demographic variables. Over the following academic year, in the 2nd phase of the study, a subsample was selected formed by subjects at risk of mood and anxiety disorders according to their cut-off scores in the screening tests (SCARED, CDI and/or LOI-CV). Additionally, we selected controls with the same age and gender characteristics, but without risk scores on any test. In the 2nd phase the SCARED, CDI and LOI-CV were re-administered to the children and teachers answered questions about academic performance. Finally in the 3rd phase we invited all subjects of the 2nd phase to participate and conducted a retest with the SCARED and the LOI-CV. We also administered the YI-4 in order to evaluate psychopathology. Parents also informed about the academic performance of their children. The participants completed the questionnaires in small groups of three or four and the investigators were present to instruct the children on how to answer the surveys. Figure 1 summarizes the study design and the sample recruitment.

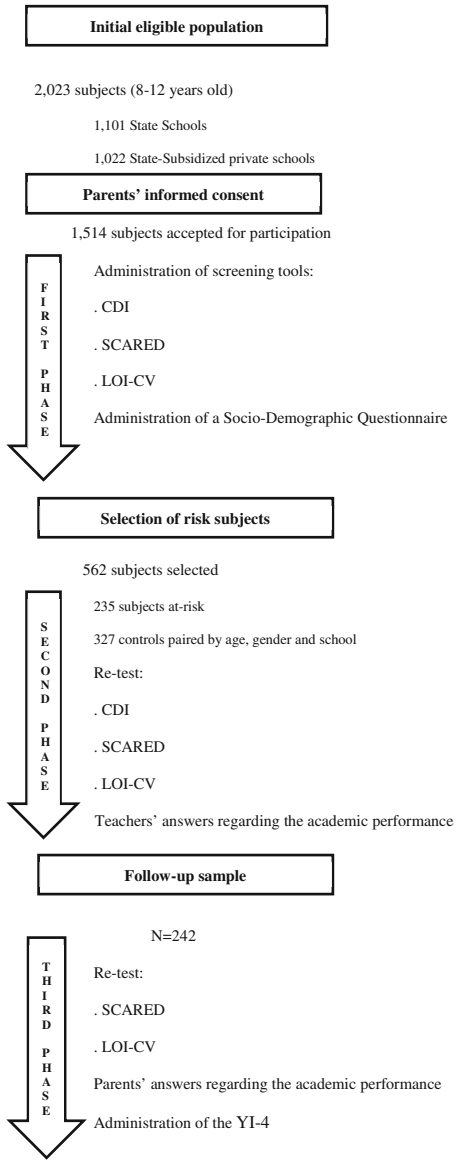


**Fig. 1** Study design

## Data Analysis

A series of statistical analyses were performed using SPSS software version 19.0.

The Chi square statistical test was used to study possible socio-demographic differences between the risk-group and the control-group subjects, and also between the subjects who participated in the 3rd phase and those who dropped out in the last phase of the study.

*t* Test analyses were used to find possible differences between two independent groups, and ANOVA was used to find possible differences between three independent groups. In particular, *t* test analyses were used to assess the relationship between various socio-demographic variables—gender: boys/girls; birthplace: foreign/native; family type: single parent/nuclear; and academic performance: low/high—and LOI-CV total and factor scores. ANOVA was used to test the possible relation between SES (high, medium or low), and LOI-CV total and factor scores. *T* test analyses and ANOVA were performed for each phase of the study.

Repeated-measures MANOVA (controlling for age and gender) was used to examine the evolution of the LOI-CV total and factor scores, over the three phases among the subjects who participated.

In order to observe the predictors of the OC manifestations (obsessiveness and OC symptomatology) in the 3rd phase, logistic regression models using the stepwise method, were performed. Both regression models were performed in three steps. The candidate variables entered into the model in the first step were: psychopathological variables of the 1st phase (LOI-CV factors scores, SCARED factors scores, and CDI total score) and socio-demographic variables such as gender and age. In the second step we added to the candidate variables of the first step: psychopathological variables of the 2nd phase (LOI-CV factors scores, SCARED factors scores, and CDI total score). In the third step we added the SCARED factors scores of the 3rd phase and the scores of the nine YI-4's categories. We adjusted the model for SES because there were significant differences between the subjects who participated in the last phase of the study and the subjects who declined to participate. Before performing the regression models, collinearity between the variables was assessed and analyses show that the LOI-CV total score was collinear with LOI-CV factors scores, and the SCARED total score was also collinear with the SCARED factors scores, so we selected the LOI-CV and the SCARED factors scores instead of the total scores.

Bonferroni correction was applied to control the increase in type I error caused by multiple comparisons, which meant that we used a significance level of .01.

## Results

### Descriptive Data of the LOI-CV Scores for the Socio-Demographic Variables per Phase of the Study

*t* Test analyses only showed some trends. Females obtained higher scores for order/checking/pollution factor (mean score = 7.33, SD = 5.4) than males (mean score = 6.76, SD = 5.2) ($t = -2.08$, $p = .037$), whereas males obtained higher scores for superstition/mental compulsion factor (mean score = 2.65; SD = 3.4) than females (mean score = 2.31, SD = 3.0) ($t = 1.99$, $p = .046$). Results also showed that subjects with single-parent families obtained higher scores (mean score = 2.94, SD = 3.8) than subjects with nuclear families (mean scores = 2.39, SD = 3.1) for superstition/mental compulsion factor ($t = 2.03$, $p = .044$). In the 3rd phase subjects with lower academic performance tended to obtain higher total scores on the LOI-CV (mean score = 17.78, SD = 12.3) than subjects with higher academic performance (mean score = 13.45, SD = 9.38) ($t = -1.97$, $p = .05$).

The ANOVA showed significant differences in the 1st phase of the study. Thus, LOI-CV scores were found to be inversely related to SES for order/checking/pollution ($F = 7.54$, $p = .001$) and superstition/mental compulsion factors ($F = 8.37$, $p = .0001$), and total score ($F = 7.62$, $p = .001$).

### Clinical and Epidemiological Evolution of the OC Manifestations

Repeated-measures MANOVA showed that scores for the LOI-CV (factors and total) significantly decreased over time independently of age and gender (Table 1).

For the two levels of severity of the OC manifestations (obsessiveness and the OC symptomatology) we obtained an obsessiveness prevalence of 30.4 % (95 % CI 28.4–33.1, N = 459) with no differences between boys and girls. The prevalence of the OC symptomatology was 4.8 % (95 % CI 3.7–5.9, N = 71) [1] and also no significant differences were found in terms of gender.

Table 2 shows the persistence, recurrence and incidence of the two levels of OC manifestations at different points

**Table 1** Evolution of the LOI-CV scores: MANOVA

| | Phase 1 mean (SD) | Phase 2 mean (SD) | Phase 3 mean (SD) | F(*p*) |
|---|---|---|---|---|
| Factor 1: order/checking/pollution | 8.87 (5.9) | 6.30 (4.0) | 6.01 (4.7) | 23.80 (.0001) |
| Factor 2: obsessive concern | 8.75 (5.6) | 6.32 (4.4) | 6.14 (4.8) | 21.95 (.0001) |
| Factor 3: superstition/mental compulsion | 3.24 (3.6) | 1.80 (2.6) | 1.55 (2.9) | 26.74 (.0001) |
| Total score | 20.86 (12.6) | 14.49 (9.0) | 13.72 (10.38) | 35.79 (.0001) |

**Table 2** Frequencies of persistence and incidence of two levels of OC manifestation severity during the different phases of the study

| | Obsessiveness % (95 % CI) | OC symptomatology % (95 % CI) |
|---|---|---|
| Persistence rate over one year (1st phase–2nd phase) | 28.4 (22.2–34.5) | 9.3 (.6–18) |
| Persistence rate over three years (1st phase–2nd phase–3rd phase) | 14.8 (8.1–23.9) | 14.3 (1.8–42.8) |
| Recurrence rate (1st phase–3rd phase) | 21.6 (14–29.3) | 15.8 (3.4–39.6) |
| Annual incidence rate (1st phase–2nd phase) | 14.4 (9.4–19.3) | 1.1 (.3–2.8) |
| Incidence rate over three years (1st phase–2nd phase–3rd phase) | 10.3 (4.5–19.2) | 1.2 (.2–4.3) |

Obsessiveness: using a LOI-CV cut-off point of 21 taking into account answers relate to presence (yes) or absence (no) of the manifestation plus the interference scores (1st phase N = 459; 2nd phase N = 89; 3rd phase N = 49)

OC symptomatology: using a cut-off point of interference score of 25 in the LOI-CV (1st phase N = 71; 2nd phase N = 8; 3rd phase N = 6)

during the follow-up. When subjects obtained scores above the cut-off point in the 1st phase of the study and also in the 2nd phase, we regarded this as the persistence rate over 1 year; and when subjects obtained scores above the cut-off point in the 1st phase, in the 2nd phase and also in the 3rd phase, we regarded this as the persistence rate over 3 years. When a subject obtained a score above the cut-off point in the 1st phase and in the 3rd phase of the study, but not in the 2nd phase, we regarded this as the recurrence rate. When subjects obtained a score below the cut-off point in the 1st phase and above the cut-off point in the 2nd phase we regarded this as annual incidence rate; and when subjects only scored above the cut-off point in the 3rd phase of the study and not in the 1st and in the 2nd phase we regarded this as the incidence rate over 3 years.

### Predictive Factors of the Two Types of OC Manifestations

To predict the obsessiveness in the 3rd phase (see Table 3), in step 1 we entered the psychopathological variables collected in the 1st phase (LOI-CV factors scores, SCARED factors scores and CDI total scores) and gender and age of subjects. We observed that separation anxiety factor of the SCARED was a good predictor and that the model explained 8.6 % of the obsessiveness. In the second step we added the psychopathological variables collected in the 2nd phase and the scores on order/checking/pollution factor and the scores on the superstition/mental compulsion factor were the best predictors. This model explained 33.1 % of the obsessiveness. Finally when we added the psychopathological variables collected in the last phase of the study to the candidate variables of the previous steps, the best predictors were the scores for the order/checking/pollution factor of the 2nd phase LOI-CV, the social phobia scores obtained in the SCARED of the 2nd and 3rd phase, and also the separation anxiety factor of the 3rd phase SCARED. These variables and the score of the schizoid personality disorder obtained from the YI-4 explained 53.3 % of the obsessiveness.

The results showed that in the first step the best predictors for OC symptomatology in the 3rd phase were separation anxiety factor and order/checking/pollution factor, and the model explained 34.6 % of the OC symptomatology. In the second step when we added the variables collected in the 2nd phase we observed that the best predictors were superstition/mental compulsion and the score of the CDI, both from the 2nd phase. The model explained a 64.5 % of the OC symptomatology. Finally in the last step we found that the best predictors were again the superstition/mental compulsion factor and the CDI total score of the 2nd phase. The model explained a 61.9 % of the OC symptomatology.

## Discussion

This study used the LOI-CV to examine prospectively the OC manifestations in a school age community sample.

Statistical trends have been found for the relationship between the scores on the LOI-CV and some socio-demographic variables in each phase of the study, and these could be due to the sample sizes. Consequently, children who came from environments where the SES was lower had higher scores on the LOI-CV. These differences were significant in the 1st phase due probably to the large sample size. The present results support those of Heyman et al. [19], but do not coincide with data from Degonda et al. [18], who concluded that individuals with OC symptoms were raised in significantly higher social classes than controls. On the other hand, in contrast with Van Oort et al. [47] we did not find that SES was a risk indicator. As for the other socio-

**Table 3** Significant regression models of prediction obsessiveness and OC symptomatology in the 3rd phase

| | Obsessiveness | | OC symptomatology | |
|---|---|---|---|---|
| | Odds ratio (95 % CI) | *p* | Odds ratio (95 % CI) | *p* |
| *Step 1* | | | | |
| LOI-CV 1st phase order/checking/pollution | – | | 1.152 (1.001–1.326) | .04 |
| SCARED 1st phase separation anxiety | 1.138 (1.052–1.233) | .001 | 1.355 (1.075–1.707) | .01 |
| | $R^2$ Negelkerke*100 = 8.6 | | $R^2$ Negelkerke*100 = 34.6 | |
| | $\chi^2_{2.235} = 13.012$ | | $\chi^2_{3.235} = 17.876$ | |
| | $p = .001$ | | $p = .001$ | |
| *Step 2* | | | | |
| LOI-CV 2nd phase order/checking/pollution | 1.201 (1.070–1.348) | .002 | – | |
| LOI-CV 2nd phase superstition/mental compulsion | 1.355 (1.140–1.609) | .001 | 1.749 (1.169–2.616) | .006 |
| CDI 2nd phase | – | | 1.201 (1.034–1.396) | .017 |
| | $R^2$ Negelkerke*100 = 33.1 | | $R^2$ Negelkerke*100 = 64.5 | |
| | $\chi^2_{3.177} = 40.914$ | | $\chi^2_{3.177} = 31.993$ | |
| | $p = .001$ | | $p = .001$ | |
| *Step 3* | | | | |
| LOI-CV 2nd phase order/checking/pollution | 1.339 (1.157–1.549) | .001 | – | |
| LOI-CV 2nd phase superstition/mental compulsion | – | | 1.645 (1.128–2.400) | .01 |
| SCARED 2nd phase social phobia | .703 (.559–.884) | .003 | – | |
| SCARED 3rd phase social phobia | 1.350 (1.089–1.674) | .006 | – | |
| SCARED 3rd phase separation anxiety | 1.359 (1.150–1.606) | .001 | – | |
| CDI 2nd phase | – | | 1.193 (1.030–1.383) | .019 |
| YI-4 schizoid personality disorder | 1.998 (1.104–3.615) | .022 | – | |
| | $R^2$ Negelkerke*100 = 53.3 | | $R^2$ Negelkerke*100 = 61.9 | |
| | $\chi^2_{6.160} = 64.057$ | | $\chi^2_{3.160} = 26.075$ | |
| | $p = .001$ | | $p = .001$ | |

* Models were adjusted for SES

Candidate variables to enter into the step 1: 1st phase LOI-CV factors scores → order/checking/pollution, obsessive concern, and superstition/mental compulsion; 1st phase SCARED factors scores → somatic/panic, social phobia, generalized anxiety, and separation anxiety; 1st phase CDI (total score); gender (1: boy; 2: girl); and age (years)

Candidate variables to enter into the step 2: At the step1 we added the 2nd phase LOI-CV factors scores → order/checking/pollution, obsessive concern, and superstition/mental compulsion; 2nd phase SCARED factors scores → somatic/panic, social phobia, generalized anxiety, and separation anxiety; and 2nd phase CDI (total score)

Candidate variables to enter into the step 3: At the step 2 we added the 3rd phase SCARED factors scores → somatic/panic, social phobia, generalized anxiety, and separation anxiety; and the nine YI-4 categories (total scores)

demographic variables, the data did not support our hypothesis, which indicates that OC manifestations could be relatively independent of socio-cultural features.

It has been reported that there are some inconsistent results regarding the age variable; while some studies note that older subjects present more OC symptoms [19, 48] other studies such as the one by Zohar and Bruno [49] have found the opposite result. Similarly our results reflect a general decrease of the LOI-CV scores over the three phases. We found that this decrease over time was not related to the sex of the participants and was also independent of the subjects' age at the beginning of the study. These results suggest some interpretations; for example the decrease in the scores may be because OC manifestations decrease with age. Likewise, there may be methodological reasons that would mean that younger subjects would be more likely to exaggerate the severity of their symptoms in the questionnaire, or that the answers in the retest may be attenuated, although this possible statistical effect is taken into account by the repeated measures MANOVA.

We did not find any significant differences between genders in the LOI-CV total scores in any phase of the study nor in obsessiveness and OC symptomatology prevalence. Our data does not support those of other studies of non-clinical samples that reported more symptoms and interference in females than in males [3, 14]. Also the present results did not support those from clinical samples that indicate a certain propensity towards OCD in adult

women and in male children and adolescents [50, 51]. However, some gender differences in clinical manifestations were observed; that is, superstition/mental compulsion symptoms were found more often in males whereas females obtained higher scores for the order/checking/pollution factor. Similarly, Maggini et al. [14] found a certain preponderance of males in items related to superstition symptomatology. The superstition/mental compulsion factor was also a predictor of the obsessiveness and OC symptomatology over the long term. Consequently, we suggest that it is important to take into account symptoms related to superstition because although it may be a manifestation that can go unnoticed or be considered milder, we have shown that it is closely related to the subclinical diagnosis of OCD [52].

The association between early anxiety and the OC manifestations might support the comorbid relationships among these symptoms; specifically the most significant anxiety manifestations were separation anxiety and social phobia. In this regard, Angst et al. [53] found that in adults the prevalence of OCD was significantly increased if the subject also had social phobia and the recent study of Assunçao et al. [54] also found higher rates of comorbidity between OCD and social phobia. Furthermore, in this early developmental stage, one of the most frequent disorders is the separation anxiety; indeed, Mroczkowski et al. [55] stated that this disorder has been shown to have a clear influence on the course of OCD, which may even mean that it is difficult to distinguish the symptomatology qualities of one from the other. In our data, separation anxiety appeared as a predictor for the two severity levels of OCD, which indicates that anxiety symptomatology may be a pre-existing feature in OCD development. In this regard, in the recent study by Jakubovski et al. [56] the OCD presented a worse prognosis when there was a family history of anxiety disorders. The data presented have also shown a relation between depression and OC symptomatology, as is the case in other studies [1, 28]. This predictive relation was observed for the severest category of OC (OC symptomatology and not for obsessiveness) which suggests that depression symptoms are due to the distress caused by the day-to-day impairment of the obsessions and compulsions in children's lives, as shown in previous studies [57]. Likewise, the results have shown a significant and positive relation between the schizoid personality disorder symptoms and obsessiveness, probably because in many cases it would be difficult to make a distinction between obsessions and delusions, as was observed Joo [58].

Results of persistence and incidence were hardly comparable to those of other studies because the design and the methodology are very different. Despite this, we did not find low rates of incidence as is the case in other studies [59, 60]. Our data have shown significant rates of incidence that we believe show the emergence of new cases in the age period studied. Moreover, although data show a significant pattern of symptom quantitative reduction over time, the rates of persistence both for obsessiveness and for OC symptomatology (around 30 %), indicate that OCD presents continuity over time within a clinical spectrum and therefore could be chronic in the long term for some cases, as we hypothesized. Also, for recurrence our findings showed high rates demonstrating that within the chronicity, the OCD can be fluctuating or episodic [10, 61]. Furthermore, the results relate to persistence rates in the two levels of severity and the predictors support the importance of taking into account the two LOI-CV cut-off points. In addition, our data were consistent with those from the meta-analysis by Stewart et al. [62] in that rates of persistence for full OCD ranged from 13 to 87 % and for subclinical OCD ranged from 17 to 46 %. Heyman et al. [63] also found that many adults recognized that the symptoms began in childhood and adolescence and Jakubovski et al. [56] found a worse prognosis associated with an earlier age of OCD onset.

This work has certain limitations that should not be overlooked. One limitation is the use of self-informant questionnaires, which runs the risk of responders misunderstanding some questions, or of having poor or limited insight into their condition. It is common in OCD cases for subjects and especially young subjects not to recognize their obsessions or compulsions as excessive or unreasonable [64]. Another limitation is that the study did not control for whether the subjects had been treated in any of the three phases, and this may interfere in the interpretation of the results obtained by the repeated-measures MANOVA. Thirdly, the major limitation is that despite the efforts of the researchers, the study suffered from reduced parental consent in the last phase. However, no differences were found between the emotional and the socio-demographic characteristics of subjects who participated and those who did not, and SES differences were controlled in the regression models. Despite these limitations, we have obtained data from a large sample followed-up at three key points in the early adolescence period and the findings indicate continuous OC manifestations and the possible occurrence of new cases during this period. The chronic evolution of the OC manifestations shows that they present recurrences and fluctuations in their level of severity, which supports the OCD spectrum. In this regard, the two levels of severity of OC manifestations were predicted by factors such as previous anxiety, previous OC manifestations or depressive symptomatology. Specifically, the less severe form of OC (obsessiveness) was related more to anxiety symptoms and OC symptoms, whereas the more severe form of OC (OC symptomatology) was related more to previous OC manifestations and depressive symptoms.

We think that more prospective and large follow-up studies need to be carried out to support to the data presented.

## Summary

In this study we aimed to explore prospectively the clinical course of OC manifestations using the LOI-CV. The questionnaire was administered to a non-clinical sample of school-age children at three points in their development. From an initial sample of 1,514 subjects (aged between 8 and 12) who underwent symptoms screening for OCD (LOI-CV), anxiety (SCARED) and depression (CDI), 562 subjects (risk group and without risk group) were re-assessed in the 2nd phase (1st phase, 2006/2007 academic year; 2nd phase, 2007/2008 academic year). 242 subjects were monitored at 3 years (3rd phase, 2009/2010 academic year). Relationships between the LOI-CV scores and socio-demographic factors were explored as well as the evolution of the LOI-CV scores over the three phases. LOI-CV scores significantly decreased over time independently of age and gender. On the other hand, we did not observe conclusive results for the association between socio-demographic variables and OC manifestations. The prevalence, persistence and incidence for two levels of severity of OC manifestations (obsessiveness and OC symptomatology) ranged between 4.8 and 30.4 %, 9.3 and 28.4 % and between 1.1 and 14.4 %, respectively. Also, 15.8 % of OC symptomatology and 21.6 % of obsessiveness presented remission and subsequent recurrence. Logistic regression models showed that between 34.6 and 64.5 % of OC symptomatology was predicted by previous OC symptoms and previous anxiety and depressive symptoms. For the obsessiveness, the depressive symptoms were not significant predictors. Our data support a substantial continuity of the OC manifestations during the period studied and the existence of different levels of severity within the OCD spectrum. We suggest that early recognition of anxiety, depression and OC symptoms may help to prevent chronicity and worse prognosis of OCD.

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## 5.3. Estudi de la trajectòria de l'ansietat autoinformada a partir del seguiment d'una mostra comunitària d'adolescents


**The developmental trajectory of self-reported anxiety symptomatology in non-clinical early adolescents: a three-year follow-up study**

Núria Voltas, Carmen Hernández-Martínez, Victoria Arija, Josefa Canals

**INFORMACIÓ REVISTA:**

*The Journal of Early Adolescence*

FI 2012: 1,686; 2Q Family studies - 3Q Psychology Developmental

**Sotmès a la revista**

**Resum:** Més d'un 50% dels subjectes presenten símptomes d'ansietat als tres anys de seguiment. Els símptomes de fòbia social són els més prevalents (55,6%), persistents (46,8% - 68,9%) i incidents (26% - 40,7%) a la població estudiada, seguits dels símptomes d'ansietat generalitzada (prevalença: 44,4%; persistència: 41% - 63%; incidència: 26,2% - 34,8%). Tanmateix, s'observa de manera consistent que són les nenes les que presenten unes majors taxes de prevalença, persistència i incidència pel que fa a aquests tipus d'ansietat. En canvi, el sexe masculí apareix com un factor protector dels símptomes crònics d'ansietat.

D'altra banda, a més a més de la fòbia social i de l'ansietat generalitzada, l'ansietat de separació també és un factor predictor de l'ansietat crònica; com també s'ha observat que els subjectes que presenten ansietat de separació persistent, són els que presenten més símptomes psicopatològics associats.

UNIVERSITAT ROVIRA I VIRGILI
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Núria Voltas Moreso
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# The developmental trajectory of self-reported anxiety symptomatology in non-clinical early adolescents: a three-year follow-up study



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| | |

# The developmental trajectory of self-reported anxiety symptomatology in non-clinical early adolescents: a three-year follow-up study

## Abstract

This study examined the course of anxiety in a non-clinical sample. Using a prospective design, 1,514 scholars (mean age=10) underwent anxiety and depression screening in the first phase. 562 subjects (risk group/without risk group) participated in the second phase and 242 were followed up after two years. The *Screen for Child Anxiety Related Emotional Disorders* was administered in the three times. The prevalence of anxiety symptoms was higher in girls (51.4%) than boys (41.5%). More than 50% of subjects maintained the anxiety symptoms, and male gender was a protective factor of persistence. Social phobia (SP) and generalized anxiety (GA) manifestations were the most prevalent and persistent. SP, GA, separation anxiety (SA) and depressive symptoms were predictors of the anxiety's continuity. Subjects with persistent SA presented the highest rates of co-occurrence and manifestations of depressive disorders were the most co-occurrent. The data support chronicity of the anxiety between childhood and adolescence.

**KEYWORDS:** anxiety symptoms, SCARED, early adolescence, prospective study.

## Introduction

Anxiety disorders are considered the most common mental health problems in childhood and adolescence, and seem to be one of the earliest forms of psychopathology (Beesdo, Knappe, & Pine, 2009). Unfortunately, anxiety symptoms and other internalizing problems are not as overt as externalizing problems, and therefore have a higher risk of not being detected (Bettge, Wille, Barkmann, Schulte-Markwort, & Ravens-Sieberer, 2008). Despite this, several epidemiological studies of preadolescents from different countries have reported that the prevalence for any anxiety disorder ranges from 2% to 32% (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Ford, Goodman, & Meltzer, 2003; Merikangas et al., 2010). In Spain, the prevalence of anxiety symptoms reached 47% (Romero-Acosta et al., 2010).

In the literature, many variables have been identified as playing an important role in the early development and maintenance of anxiety: these include genetic and environmental variables such as an overprotective parental style, an insecure attachment, parental health problems, parental income, or having experienced a stressful life event (Allen, Rapee, & Sandberg, 2008; Eley & Gregory, 2004; Franic, Middeldorp, Dolan, Ligthart, & Boomsma, 2010; Rapee, 1997; Van Oort, Greaves-Lord, Ormel, Verhulst, & Huizink, 2011; Warren, Huston, Egeland, & Sroufe, 1997). Moreover, some studies have assessed the effect of gender and age on the expression and development of anxiety at early stages. Girls tend to have more anxiety symptoms than boys for all anxiety disorders. These gender differences may occur early in childhood, may increase with age, and may be observed across different cultures (Beesdo et al., 2009; Craske, 2003; Essau, Muris, & Ederer, 2002; Essau, Sakano, Ishikawa, & Sasagawa, 2004; Muris, Schmidt, Engelbrecht, & Perold, 2002). Regarding age, Kessler et al. (2005) concluded that the mean age of onset for the anxiety disorders was 11 years-old. Although it is normal for children to experience some degree of worries or fears in certain situations, these authors suggested that it is especially necessary to consider children who present anxiety symptoms which cause them important distress in their daily functioning. Also, in early adolescence, anxiety disorders can potentially have a negative impact on social, family and academic function causing low self-esteem at a time marked by considerable transition (Lundy, Silva, Kaemingk, Goodwin, & Quan,

2010; Maldonado et al., 2013; Rapee, Schniering, & Hudson, 2009). In addition, in a recent study Essau, Lewinsohn, Olaya, and Seeley (2014) found that adolescent anxiety is associated with adverse psychosocial outcomes at the age of 30, and for this reason we believe that it is important to examine the characteristics of anxiety manifestations in the period of early adolescence. Sometimes, for some anxiety disorders an earlier age of onset has been associated with greater severity and a worse course (Ramsawh, Weisberg, Dyck, Stout, & Keller, 2011). In this regard, separation anxiety and some types of specific phobias have been observed with an earlier age of onset than generalized anxiety and panic disorders (Kessler et al., 2005; Becker et al., 2007). However, findings related to the age of onset are inconsistent (Beesdo et al., 2009; Burstein, Kattan, Albano, Avenevoli, & Merikangas, 2011). The variability of the results may therefore be due to cultural factors or to secular changes. On the other hand, an early onset of anxiety has also been related to increased co-occurrence with other disorders (Campbell, Brown, & Grisham, 2003; Iketani et al., 2004). In fact, previous studies have found that lifetime comorbidity in patients with anxiety disorders occurs in more than 80% of cases (Brown, Campbell, Lehman, Grisham, & Mancil, 2001). For example, anxiety symptoms and eating disorder symptoms may be comorbid (Hughes, 2012), and anxiety has also been related to an increase in body mass index (BMI) in both children and adolescents (Aparicio, Canals, Voltas, Hernández-Martínez, & Arija, 2013; Hillman, Dorn, & Bin, 2010). Moreover, the co-occurrence of anxiety with conduct problems, or with symptoms of bipolar disorder, attention deficit hyperactivity disorder (ADHD), tic disorder and somatic complaints, also affects substantial proportions of children and adolescents and this may involve the emergence of associated problems in future stages of development. (Cunningham & Ollendick, 2010; Copeland, Angold, Shanahan, & Costello, 2014; Dufton, Dunn, & Compas, 2009; Sala et al., 2010; Schatz & Rostain, 2006; Schneider, Gadow, Crowell, & Sprafkin, 2009). And it has also been found that the co-occurrence of anxiety and depression seems to be particularly frequent (Masi et al., 2004; Mathew, Pettit, Lewinsohn, Seeley, & Roberts, 2011) and it is a consistent predictor of more severe symptomatology, adverse treatment results, family dysfunction problems, and chronicity (Guberman & Manassis, 2011; Lamers et al., 2011; Rapee et al., 2009; Rapee et al., 2013).

To date, although there are some follow-up epidemiologic studies among children and adolescents from the community, the adolescent course of anxiety symptoms is still poorly understood (Côté, Boivin, Liu, Nagin, Zoccolillo, & Tremblay, 2009; Gullone, King, & Ollendick, 2001; Hale III, Raaijmakers, Muris, van Hoof, & Meeus, 2008; Van Oort, Greaves-Lord, Verhulst, Ormel, & Huizink, 2009; Leikanger & Larsson, 2012). In general, studies suggest that anxiety symptoms present a continuous course throughout development, although in varying degrees of severity. Concretely, it seems that anxiety symptoms tend to increase in frequency over the first five years of life (Côté et al., 2009), decrease during early adolescence and subsequently increase from middle to late adolescence (Van Oort et al., 2009). Another issue is contributing to an early detection of the anxiety manifestations and having the appropriate tools to facilitate an early and swift recognition. Some authors have provided tools that were developed taking into account factors that are directly related to the DSM-IV-TR anxiety disorders (Birmaher et al., 1997; March, Parker, Sullivan, Stallings, & Conners, 1997; Silverman, Fleisig, Rabian, & Peterson, 1991). In specific terms, the questionnaire developed by Birmaher et al. (1997), the Screen for Child Anxiety Related Emotional Disorders (SCARED), has been considered one of the best multidimensional anxiety disorder symptom questionnaires (Myers & Winters, 2002).This questionnaire is currently widely used (Crocetti, Hale III, Fermani, Raaijmarkers, & Meeus, 2009; Hale III, Crocetti, Raaijmakers, & Meeus, 2011; Leikanger & Larsson, 2012) and in a recent study we were able to prove that the SCARED is a useful, valid, and reliable self-report instrument for predicting and screening anxiety symptoms in a community school-age sample (Canals, Hernández-Martínez, Cosi, & Domènech, 2012; Vigil-Colet et al., 2009).

Taking all the above into account, there are various reasons for our interest in analysing the course of anxiety in early adolescence. First, anxiety symptoms interfere considerably in the daily lives of subjects and especially during the transition to adolescence. And second, we wish to provide greater insight into the course of anxiety and related factors in a period in which this issue has been little studied. The aims of this prospective study were therefore: 1) to determine the course of anxiety symptoms in early adolescents, controlling for age, gender and socioeconomic status (SES) 2) to determine the course taken by the anxiety symptoms by estimating their prevalence,

persistence, recurrence, and incidence, 3) to examine the co-occurrence of psychopathological symptoms and school-social impairment in chronic anxiety, and 4) to explore the predictive psychopathological, socio-demographic, and anthropometric factors of persistent anxiety symptoms in the long term. We hypothesized that anxiety manifestations will have a chronic course during early adolescence, they will be more prevalent in girls than in boys, and that the evolution of the manifestations will differ according to anxiety categories.

## Method

*Participants*

A three-year follow-up study was conducted of 242 school-age children. The participants were recruited from a three-phase epidemiological study of anxiety and depression disorders that was begun in 2006/2007 academic year in the town of Reus (Spanish town of 100,000 habitants).

The baseline sample in the study was a group of 1,514 children (720 boys) in the fourth, fifth and sixth grades of primary school with a mean age of 10.23 (*SD*=1.23). Subjects came from thirteen schools randomly chosen from the town's state schools and state-subsidized private schools. A total of 39.5% of the children belonged to families with a low SES, 42.5% to families with a medium SES and 18% to families with a high SES. 87.5% of the sample was born in Spain, and 85.9% belonged to a nuclear family. Once we had screened the first phase, 562 students (254 boys) with a mean age of 11.25 (*SD*=1.04) were selected to participate in the second phase as subjects at risk of anxiety or depression disorders (72.1%) or as members of a control group without risk (27.9%). Two years later, all 562 subjects were invited to participate in the third phase follow-up, and 242 subjects (95 boys) with a mean age of 13.52 (*SD*=.94) participated. No differences were found between the psychopathological scale scores of subjects who participated in the third phase and subjects who dropped out of the study, or between these two groups and socio-demographic variables such as gender, birthplace or family type. However, there were differences related to the SES factor: low SES participants

were associated with higher dropout rates than medium or high SES participants (Chi-square$_{2.561}$=13.557; p=.001).

*Measures*

***Screen for Childhood Anxiety Related Emotional Disorders (SCARED) (Birmaher et al., 1997).*** SCARED is a self-report questionnaire that assesses anxiety disorder symptoms in subjects aged 8 to 18. SCARED is composed of 41-items, and subjects are asked about the frequency of each symptom using a 3-point response format: 0 (almost never), 1 (sometimes), 2 (often). The reliability of the Spanish version is α=.86, and it consists of 4 factors called somatic/panic (S/P) (12-items/α=.78), social phobia (SP) (7-items/α=.69), generalized anxiety (GA) (9-items/α=.69), and separation anxiety (SA) (13-items/α=.70) (Vigil-Colet et al., 2009). For this follow-up study, a score of 25 has been considered the cut-off point for risk of anxiety (Birmaher et al., 1997; Canals et al., 2012). Canals et al. (2012) also proposed cut-off scores for the SCARED factors with sensitivities between 74% and 78%. SCARED was administered in the three phases.

***Children's Depression Inventory (CDI) (Kovacs, 1992)***. CDI is a 27-item self-report inventory for assessing depression in subjects aged 7 to 17. Children selected the sentence from each group that best described themselves in the two previous weeks. The reliability of this version has been reported as good (α=.81 to .85) (Figueras, Amador-Campos, Gómez-Benito, & Del Barrio, 2010). CDI was administered in the first and second phase. A score of 17 was considered as the cut-off point for risk of depression (Canals, Martí-Henneberg, Fernández-Ballart, & Domènech, 1995).

***Youth's Inventory-4 (YI-4) (Gadow & Sprafkin, 1999)***. YI-4 is a self-report rating scale that evaluates DSM-IV symptoms of emotional and behaviour disorders in youths aged 12 to 18. The YI-4 contains 120-items. To obtain our results, we took the following disorders into account: ADHD–inattentive (ADHD-I), ADHD-hyperactive/impulsive (ADHD-HI), ADHD–combined (ADHD-C), conduct disorder (CD), oppositional defiant disorder (ODD), obsessions, compulsions, motor tic

disorders, vocal tic disorders, schizoid personality, schizophrenia, major depression (MD), dysthymia, bipolar disorder (BD), anorexia, bulimia, and substance use. In this study, the YI-4 demonstrated satisfactory internal consistency (α=.95). The cut-off points provided by the authors of the questionnaire were used. YI-4 was administered in the third phase.

***Anthropometry***, ***weight*** and ***height*** were individually evaluated in the first phase, and the BMI was obtained.

A ***socio-demographic questionnaire*** designed by the authors for this study was used to assess the socio-demographic characteristics of the sample. The children answered questions about age, gender, place and date of birth, family type and parental occupation. This information was corroborated by parents. The SES was established by the Hollingshead index (Hollingshead, 2011). This index allows the social status of each individual to be determined by categorizing his or her occupation into one of nine categories (from unskilled work to highly skilled work), and his or her level of education into one of seven categories (from non-completed primary education to completed higher education). The status score is estimated by multiplying the occupation scale value by a weight of five and the education scale value by a weight of three and then combining the two scores. For this study, the family SES was determined by combining the data obtained from the father and the mother. The scores range from 0 to 66, so in order to obtain three categories (low, medium and high) we considered scores lower than 22 to be low SES, scores between 23 and 44 to be medium, and scores over 44 to be high. This questionnaire was administered in the first phase.

Other socio-demographic factors were assessed in the third phase by another questionnaire designed by the authors for this study which was answered by the parents. Using this questionnaire, parents answered questions about their children's ***academic performance*** which was assessed by subjects of knowledge (language, social sciences, mathematics and natural sciences), using four scoring levels: fail, below average, average and above average. For this study, academic performance was determined by a variable with two categories: low (when the academic performance was fail or below average) and medium-high (when the academic performance was average or above average). Parents also assessed their ***children's peer relations competence*** with the

following question: *compared to other children of the same age, how does he/she behave with other children?* The answer options were worse than others, like others, and better than others. A variable with two categories was used for this study: worse than others, or like others/better than others.

*Procedure*

Before beginning the study, the project was approved by the Rovira i Virgili University ethics committee for research on individuals, and also received permission from the Ministry of Education of the Catalan Government. A representative sample of subjects was then selected, and cluster sampling was conducted by randomly selecting a set of primary schools from a total of 26 schools from all five representative areas of Reus (Spain). We then contacted the school boards and all agreed to participate. After that, a letter to all parents was sent to inform them about the study and to ask for their written informed consent.

The first phase took place during the 2006/2007 academic year; the second phase took place during the following academic year (2007/2008), and the third phase during the 2009/2010 academic year. Participants in the first phase answered screening tests for anxiety and depressive symptoms. Anthropometric data and socio-demographic data were also recorded. Over the following academic year, in the second phase, a subsample was selected consisting of subjects at risk of anxiety and depression disorders according to their cut-off point in the screening tests [SCARED cut-off point: 32, given that in the moment of the subsample selection in Spain the SCARED cut-off had not been validated yet, this score corresponded to percentile 75 of our sample, the same percentile used by Birmaher et al. (1999) in a sample of outpatients from the USA; CDI cut-off point: 17 (Canals et al., 1995); The Leyton Obsessional Inventory-Child Version (LOI-CV) cut-off point: 25 interference score (Berg, Whitaker, Davies, Flament, & Rapoport, 1988)]. Controls with the same age and gender characteristics, but without risk scores on any test were also selected. SCARED and CDI were re-administered in the second phase. Finally, in the third phase, all the subjects in the second phase were re-invited to participate and a retest with the SCARED was conducted. The YI-4 was also administered. Parents also informed about the academic performance of their

children, and about their children's social functioning. Participants completed the questionnaires in small groups and the researchers were present to instruct the children on how to answer the surveys and to resolve doubts.

*Statistical analyses*

Statistical analyses were performed using SPSS 20.0. Epidat software version 3.1 (Xunta de Galicia, Spain) was also used in order to perform the Two-proportion z-test for calculating the possible differences between genders for prevalence, persistence, recurrence, and incidence rates.

Linear mixed model analysis was performed to determine the effects on changes in outcome measures. The analysis focused on the fixed effects, considering whether there was an interaction between phase and gender, and a random effect for subject. Age and SES were included as co-variables. Significant interactions were broken down by exploring pairwise comparisons and corrected using the Bonferroni method.

The SCARED mean scores by gender obtained in each phase were calculated. An ANOVA was then performed in order to compare the mean scores obtained for boys and girls for each phase of the study.

Chi-square analyses were used in order to assess the possible relationship between the persistent or non-persistent subjects during the three phases, and whether or not they presented YI-4 symptoms, whether they had low or high academic performance, or whether they had good social functioning.

Logistic regression models using the stepwise method were performed in order to observe the predictors of the anxiety persistence rate over three years. Before performing the logistic regression models, collinearity between the variables was assessed by computing Pearson correlations with the candidate variables to enter into the models. Collinearity was deemed to have occurred when the correlations between variables were above .5. The SCARED total score was collinear with SCARED factors scores, so the SCARED factors scores were selected instead of the total score. Two

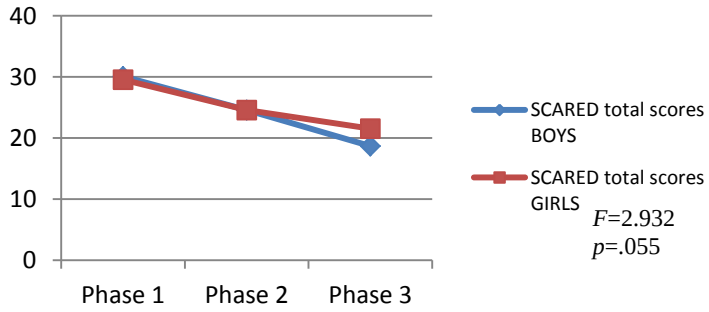
logistic regression models were therefore performed. The candidate variables to enter in model 1 were the following variables in the first phase: SCARED factor scores, CDI total score, the BMI, and socio-demographic variables such as gender, age, birthplace, and family type. The candidate variables to enter in model 2 were the same as in model 1 except for the SCARED factor scores in the first phase. All the models were adjusted for SES, because there were significant differences between the subjects who participated in the third phase of the study and those who declined to participate.

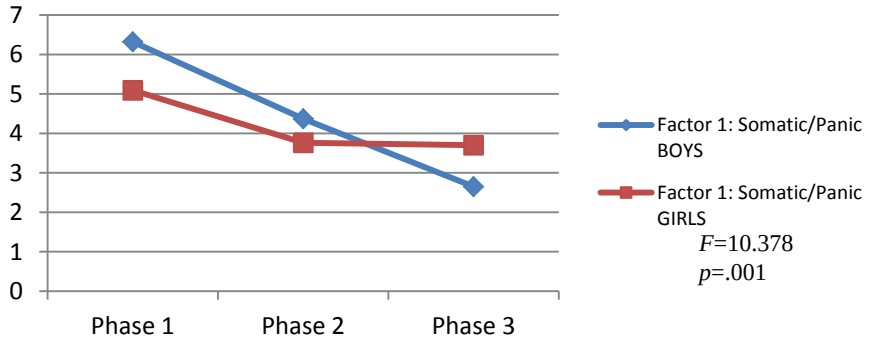
## Results

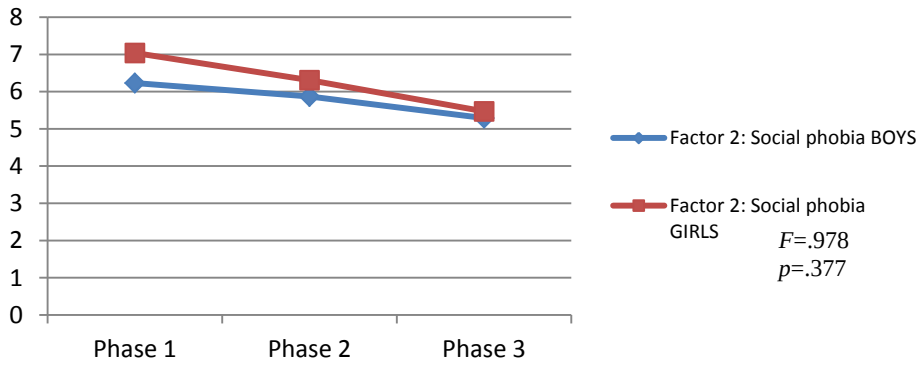
*Evolution of the SCARED scores*

Taking into account the total scores in the SCARED, the mean scores obtained by the subjects that participated in each phase were: first phase mean=24.35 (*SD*=10.34); second phase mean=24.68 (*SD*=10.63), and third phase mean=20.30 (*SD*=10.40). There were existed statistically significant differences between genders only in the first phase (boys: *M*=23.25, *SD*=10.67 and girls: *M*=25.33, *SD*=9.94; *F*=15.376, *p*=.001).

Linear mixed model analysis showed that SCARED scores decreased significantly over time (total: *F*=75.067, *p*=.001; factor 1 S/P: *F*=34.576, *p*=.001; factor 2 SP: *F*=18.377, *p*=.001; factor 3 GA: *F*=8.338, *p*=.001; factor 4 SA: *F*=134.261, *p*=.001). For factor 3 (GA) the decrease from the second to the third phase was not significant. Figure 1 shows the evolution of the SCARED scores by gender, and there were only statistically significant differences for factor 1 (S/P). However, for the total SCARED scores, girls scored significantly higher than boys in the third phase (girls: *M*=21.53, *SD*=10.4; boys: *M* =18.69, *SD*=10.6; *p*=.042). For the S/P factor boys scored higher than girls in the first phase (boys: *M* =6.32, *SD*=4.1; girls: *M* =5.09, *SD*=4.0; *p*=.023) and by contrast, girls scored higher than boys in the third phase (girls: *M* =3.70, *SD*=3.3; boys: *M* =2.65, *SD*=3.4; *p*=.018).


40
30
20
10
0
Phase 1
Phase 2
Phase 3
SCARED total scores BOYS
SCARED total scores GIRLS
F=2.932
p=.055


7
6
5
4
3
2
1
0
Phase 1
Phase 2
Phase 3
Factor 1: Somatic/Panic BOYS
Factor 1: Somatic/Panic GIRLS
F=10.378
p=.001


8
7
6
5
4
3
2
1
0
Phase 1
Phase 2
Phase 3
Factor 2: Social phobia BOYS
Factor 2: Social phobia GIRLS
F=.978
p=.377

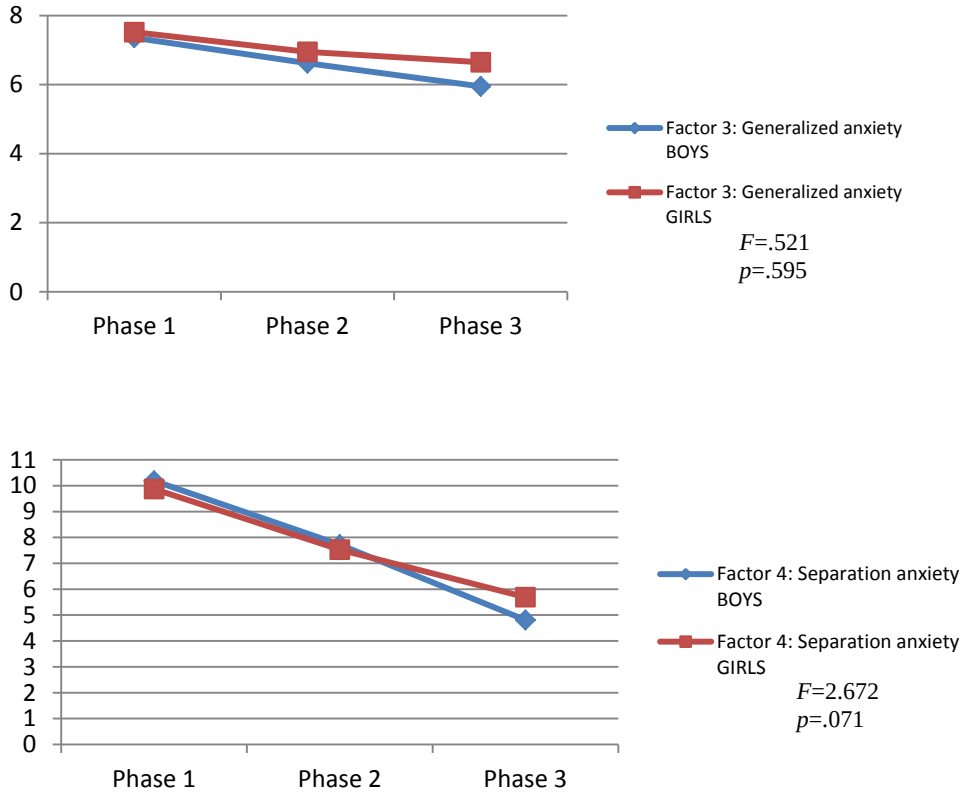



**Figure 1.** Evolution of the SCARED scores (total and factors), using an interaction term between phase and gender indicators.

*Prevalence, persistence, recurrence and incidence of anxiety symptoms*

The prevalence (first phase) of anxiety symptoms was 46.7% (CI95%:44.2-49.2) (Romero-Acosta et al., 2010). Table 1 shows the prevalence rates for factors and gender. Girls presented significantly higher prevalence rates than boys for total anxiety, SP, GA, and SA ($Z$=3.80, $p$=.0001; $Z$=5.53, $p$=.00001; $Z$=2.25, $p$=.0246; $Z$=3.33, $p$=.0009, respectively).

**Table 1.** Prevalence rates of anxiety symptoms, by gender.

| | **Factor 1** S/P | **Factor 2** SP | **Factor 3** GA | **Factor 4** SA | **Total** |
|---|---|---|---|---|---|
| **PREVALENCE RATES** | 25.1% (CI95%: 22.9 – 27.3) | 55.6% (CI95%: 53.1– 58.1) | 44.4% (CI95%: 41.9 – 46.9) | 35.1% (CI95%: 32.7 – 37.5) | 46.7% (CI95%: 44.2 – 49.2) |
| Boys | 23.7% (CI95%: 20.6 – 26.9) | 48% (CI95%: 44.4 – 51.7) | 41.3% (CI95%: 37.7 – 44.9) | 30.7% (CI95%: 27.3 – 34.1) | 41.5% (CI95%: 37.9 – 45.1) |
| Girls | 26.3% (CI95%: 23.3 – 29.4) | 62.3% (CI95%: 59 – 65.7) | 47.2% (CI95%: 43.8 – 50.7) | 39% (CI95%: 35.6 – 42.4) | 51.4% (CI95%: 47.9 – 54.9) |

Table 2 show the persistence, recurrence, and incidence rates. When subjects obtained scores above the total SCARED cut-off point in the first phase (1) as well as in the second phase (1), we regarded this as the persistence rate over one year (1/1); and when subjects obtained total scores above the cut-off point in the first phase (1), in the second phase (1) and also in the third phase (1), we regarded this as the persistence rate over three years (1/1/1). When subjects obtained a total score above the SCARED cut-off point in the first phase (1), and in the third phase (1) but not in the second phase (0), we regarded this as recurrence rate over three years (1/0/1). When subjects obtained a total score below the SCARED cut-off point in the first phase (0) and above the cut-off point in the second phase (1) we regarded this as the annual incidence rate (0/1); and when subjects only scored above the SCARED cut-off point in the third phase (1) of the study and not in the first (0) and in the second phase (0) we regarded this as the incidence rate over three years (0/0/1).

**Table 2.** Persistence, recurrence, and incidence rates of anxiety symptoms during the follow-up, by gender.

| | **Factor 1** S/P | **Factor 2** SP | **Factor 3** GA | **Factor 4** SA | **Total** |
|---|---|---|---|---|---|
| **PERSISTENCE RATE OVER ONE YEAR** (1/1) (first phase/second phase) | 39.6% (CI95%: 33.5 - 45.7) | 68.9% (CI95%: 64.1 – 73.7) | 62.9% (CI95%: 57.7 – 68.1) | 45% (CI95%: 39.5 – 50.5) | 56.4% (CI95%: 51.3 – 61.3) |
| Boys | 34.6% (CI95%: 33.5 – 45.7) | 61.9% (CI95%: 53.7 – 70.2) | 54.4% (CI95%: 46 – 62.7) | 42.9% (CI95%: 34.2 – 51.5) | 51.6% (CI95%: 43.7 – 59.6) |
| Girls | 43.3% (CI95%: 35.1 – 51.4) | 73.2% (CI95%: 67.3 - 79) | 68.9% (CI95%: 62.4 – 75.4) | 46.5% (CI95%: 39.3 – 53.7) | 59.6% (CI95%: 53.1 - 66) |
| **PERSISTENCE RATE OVER THREE YEARS** (1/1/1) (first phase/second phase/third phase) | 19.2% (CI95%: 11.7 – 26.8) | 46.8% (CI95%: 38.9 – 54.6) | 40.9% (CI95%: 32.9 - 49) | 13.6% (CI95%: 7.8 – 19.5) | 32.3% (CI95%: 25.1 – 39.5) |
| Boys | 10.9% (CI95%: 3.6 – 23.6) | 48.9% (CI95%: 34.1 – 63.9) | 33.3% (CI95%: 20.4 – 48.4) | 8.3% (CI95%: 2.3 - 20) | 25.9% (CI95%: 15.3 - 39) |
| Girls | 25.9% (CI95%: 15.3 - 39) | 45.8% (CI95%: 36.4 – 55.2) | 44.8% (CI95%: 34.6 – 55.3) | 16.7% (CI95%: 9.4 – 26.4) | 35.9% (CI95%: 26.7 – 45.2) |
| | **Factor 1** S/P | **Factor 2** SP | **Factor 3** GA | **Factor 4** SA | **Total** |
| **RECURRENCE RATE OVER THREE YEARS** (1/0/1) (first phase/second phase/third phase) | 14.4% (CI95%: 7.7 - 21.2) | 7.8% (CI95%: 4.1 – 13.2) | 13.9% (CI95%: 8.2 – 19.5) | 6.1% (CI95%: 2.7 – 11.6) | 8.1% (CI95%: 4.4 – 13.4) |
| Boys | 10.9% (CI95%: 3.6 – 23.6) | 12.8% (CI95%: 4.8 – 25.7) | 12.5% (CI95%: 4.7 – 25.3) | 2.1% (CI95%: 0.05 – 11.1) | 5.2% (CI95%: 1.1 – 14.4) |
| Girls | 17.2% (CI95%: 8.6 – 29.4) | 5.6% (CI95%: 2.1 – 11.8) | 14.6% (CI95%: 8.2 – 23.3) | 8.3% (CI95%: 3.4 – 16.4) | 9.7% (CI95%: 4.8 – 17.1) |
| | **Factor 1** S/P | **Factor 2** SP | **Factor 3** GA | **Factor 4** SA | **Total** |
| **ANNUAL INCIDENCE RATE** (0/1) (first phase/second phase) | 15% (CI95%: 11.1 - 19) | 40.7% (CI95%: 33.9 – 47.4) | 34.8% (CI95%: 28.6 – 41.1) | 13.8% (CI95%: 9.3 – 18.3) | 21.7% (CI95%: 15.6 – 27.7) |
| Boys | 17.1% (CI95%: 11 – 23.2) | 39.7% (CI95%: 30.8 – 48.6) | 39.3% (CI95%: 30.2 – 48.3) | 13.7% (CI95%: 8.9 – 22.8) | 19.5% (CI95%: 12.2 – 28.9) |
| Girls | 13.2% (CI95%: 8 – 18.3) | 42.1% (CI95%: 31.6 - 53) | 30.4% (CI95%: 21.8 – 38.9) | 13.8% (CI95%: 7.7 – 19.9) | 24.1% (CI95%: 15.4 – 34.7) |
| **INCIDENCE RATE OVER THREE YEARS** (0/0/1) (first phase/second phase/third phase) | 9.5% (CI95%: 4.8 – 16.3) | 25.9% (CI95%: 15 – 39.7) | 26.2% (CI95%: 15.8 - 39) | 4.1% (CI95%: 1.1 – 10.1) | 7.7% (CI95%: 2.6 - 17) |
| Boys | 2.7% (CI95%: 0.1 – 14.2) | 25.9% (CI95%: 11.1 – 46.3) | 32% (CI95%: 14.9 – 53.5) | 5% (CI95%: 0.6 – 16.9) | 7.1% (CI95%:0.9 – 23.5) |
| Girls | 12.7% (CI95%: 6.2 – 22.1) | 25.9% (CI95%: 11.1 – 46.3) | 22.2% (CI95%: 10.1 - 39.2) | 3.4% (CI95%: 0.4 – 11.9) | 8.1% (CI95%: 1.7 – 21.9) |

The persistence rate over one year of the total score was 56.4% and females obtained higher rates, but these gender differences were not statistically significant (table 2). The persistence rate over three years was 32.3% and although also in this case the persistence was higher for girls, the differences were not significant. As shown in table 2, the highest persistence of the different factors of the SCARED for the two periods was for SP and GA. In all the factors, the frequencies of persistence were higher for girls, but significant differences between genders were found only in the persistence rate over one year for the SP factor ($Z$=2.09, $p$=.03) and for the GA factor ($Z$=2.59,

*p*=.01). On the other hand, when subjects obtained scores below the SCARED cut-off point in one of the phases, and scores were positive in the two other phases (0/1/1-1/0/1-1/1/0), the possibility that these subjects were clinically anxious for some factors was taken into account. This case was regarded as the partial persistence rate and was taken into account when subjects obtained scores above the cut-off point for any of the SCARED factors in a phase which none reached the cut-off point score of the total SCARED. Therefore we calculated a new 1/1/1 to calculate this new rate of persistence. The partial persistence rate over three years reached 55.2% (CI95%:47.6–62.8).

The recurrence rates were generally low (table 2). S/P and GA factors were the anxiety subtypes that presented the highest rates of recurrence over three years (14.8 and 13.9%), but there were no significant differences between genders in either case. Interestingly, all the subjects that presented recurrence (1/0/1) were partial persistent subjects.

Table 2 also shows that SP factor presented the highest incidence rate over one year, followed by GA. SP and GA factors presented the highest incidence rates over three years. No significant differences were found between genders.

*Co-occurrence of psychopathological symptoms and school-social impairment in chronic anxiety*

Subjects who were persistent for anxiety over the three phases of the study presented high rates of co-occurrence with YI-4 symptoms in the third phase (table 3). In specific terms, significant differences were found between subjects who presented persistence of anxiety and subjects who did not present anxiety in any phase for obsessive symptomatology, vocal tic symptoms, major depression symptoms, dysthymia symptoms, and bulimia symptoms ($\chi^2$=21.973, *p*=.001; $\chi^2$=7.272, *p*=.007; $\chi^2$=8.588, *p*=.003; $\chi^2$=8.865, *p*=.003; $\chi^2$=5.689, *p*=.017). On the other hand, subjects with SA persistence presented the highest rates of co-occurrence (between 16.7%-61.1%) for all the disorders except for schizoid personality and schizophrenia.

Moreover, significant differences were found in the academic performance variable between subjects who presented persistence rates of anxiety symptoms and subjects who presented no anxiety in any phase ($\chi^2$=4.770; $p$=.029). In specific terms, most of the subjects with high academic performance did not present anxiety persistence. No statistically significant differences were found for the social competence variable.

**Table 3.** Co-occurrence of psychopathological symptoms between anxiety persistent and non-persistent subjects.

| | Factor 1: S/P persistence | Factor 2: SP persistence | Factor 3: GA persistence | Factor 4: SA persistence | Total persistence SCARED 1/1/1 | No anxiety symptoms in any phase 0/0/0 |
|---|---|---|---|---|---|---|
| **ADHD-I** | 5% | 4.17% | 1.69% | 16.67% | 5.88% | 5% |
| **ADHD-HI** | 5% | 1.39% | 1.69% | 5.56% | 5.88% | 1.67% |
| **ADHD-C** | 0% | 0% | 3.39% | 5.56% | 1.96% | 0% |
| **Conduct disorder** | 0% | 1.39% | 3.39% | 5.56% | 1.96% | 5% |
| **Oppositional defiant disorder** | 10% | 0% | 3.39% | 16.67% | 5.88% | 0% |
| **Obsessive** | 35% | 18.06% | 25.42% | 61.11% | 35.29% | 1.67% |
| **Compulsive** | 10% | 15.28% | 13.56% | 16.67% | 13.73% | 5% |
| **Motor tics** | 30% | 16.67% | 15.25% | 33.33% | 19.61% | 10% |
| **Vocal tics** | 15% | 5.56% | 10.17% | 16.67% | 15.69% | 1.67% |
| **Schizoid personality** | 0% | 0% | 0% | 0% | 0% | 0% |
| **Schizophrenia** | 5% | 1.39% | 0% | 0% | 1.96% | 0% |
| **Major depression** | 15% | 5.56% | 10.17% | 33.33% | 17.65% | 1.67% |
| **Dysthymia** | 25% | 9.72% | 15.25% | 27.78% | 21.57% | 3.33% |
| **Bipolar disorder** | 10% | 2.78% | 3.39% | 16.67% | 5.88% | 0% |
| **Anorexia** | 1.67% | 5.56% | 5.08% | 22.22% | 7.84% | 1.67% |
| **Bulimia** | 15% | 13.89% | 13.56% | 22.22% | 19.61% | 5% |
| **Substance use** | 5% | 1.39% | 5.08% | 11.11% | 1.96% | 3.33% |

**Table 4.** Logistic regression models to predict presence of anxiety symptoms at long term.

| **Model 1** | **Persistence rate over 3 years** | |
|---|---|---|
| | **Odds Ratio (95%CI)** | ***p*** |
| SCARED first phase SP | 10.424 (1.489 - 72.991) | .018 |
| SCARED first phase GA | 8.608 (1.474 - 50.283) | .017 |
| SCARED first phase SA | 8.460 (1.518 - 47.151) | .015 |
| | $R^2$Negelkerke*100=94.9 | |
| | $\chi^2_{4.106}$=131.611 | |
| | *p*=.001 | |
| **Model 2** | | |
| | **Odds Ratio (95%CI)** | ***p*** |
| GENDER (1) | .339 (.126 - .915) | .033 |
| CDI first phase | 1.169 (1.088 - 1.257) | .001 |
| | $R^2$Negelkerke*100=31.8 | |
| | $\chi^2_{3.106}$=28.867 | |
| | *p*=.001 | |

*Models were adjusted for SES.

Candidate variables to enter into the model 1: first phase SCARED factors scores→ S/P, SP, GA, and SA; first phase CDI (total score); gender (1: boy; 2: girl); and age (years); birthplace (0: foreign; 1: native); family type (0: single parent; 1: nuclear); and first phase BMI (total score).

Candidate variables to enter into the model 2: first phase phase CDI (total score); gender (1: boy; 2: girl); and age (years); birthplace (0: foreign; 1: native); family type (0: single parent; 1: nuclear); and first phase BMI (total score).

*Predictive factors of the anxiety persistence in the third phase*

Table 4 show the logistic regression models. The variables collected in the first phase were entered in model 1: SCARED factor scores, CDI total scores, age, gender, birthplace, family type, and BMI total scores. The results show that previous anxiety manifestations were the best predictors of the anxiety persistence in the long term (the model explained 94.9%), and especially the symptoms of SP, GA, and SA.

In model 2, the SCARED factor scores were excluded from the regression model, and the persistence was only explained by 31.8%. The results showed that being a boy was a protective factor for anxiety persistence, and that high scores in the CDI were also good predictors of anxiety persistence.

## DISCUSSION

This is a follow-up study of the developmental course of several anxiety disorder symptoms in a representative community sample of early adolescents. In this study results showed that SCARED scores (factors and total) decrease during the period studied, as observed by Van Oort et al. (2009). Despite this, the data also indicated that anxiety presented a continuous course. Specifically, 56.4% of the children with anxiety symptoms persisted in the next year. However, although 32.3% of the participants presented persistence of anxiety symptomatology at the end of the three phases, this rate reaches 55.2% if partial persistence is added. Our data support those of Gullone et al. (2001) and Leikanger et al. (2012), who found stable high levels of anxiety symptoms in early adolescence. Within of the several categories of anxiety, SP presented the highest prevalence rate (55.6%), was the most persistent category in the short term (68.9%) and long term (46.8%), and also presented high rates of incidence (25.9%-40.7%). These results are in agreement with previous studies, which found that SP was highly prevalent in early adolescence and could cause significant interference in such important areas of subjects' lives as academic achievement or social relationships (Beesdo-Baum et al., 2012; Gren-Landell et al., 2009). Data also showed that previous SP symptomatology was an important predictor of anxiety persistence over time, which suggests that the early detection and treatment of this subtype of anxiety is important for preventing anxiety from becoming a chronic problem in young adulthood as discussed by Kerns, Read, Klugman, and Kendall (2013), and avoiding consequences such as the further development of

other internalizing problems or even substance abuse problems (Beesdo et al., 2007; Buckner et al., 2008). In this regard, a recent study found that feelings of loneliness may be implicated in the relationship between social anxiety symptomatology and suicidality in teens (Gallagher, Prinstein, Simon, & Spirito, 2014). For this reason, educational and clinical professionals should recognize the SP symptoms and thus ensure children's good social adjustment. In addition to the SP category, SA and GA were also found as important predictors of the anxiety persistence. Data therefore suggest that previous anxiety is the best predictor of the persistence of anxiety symptoms. Furthermore, results also showed that GA was highly prevalent, persistent, and incident, and that there was no significant decrease in the scores in the last phase. Consistent with these findings, Van Oort et al. (2009) found that there is a GA symptoms increase in adolescence, which must also be taken into account by professionals.

Regarding the gender variable, according to other findings the results showed that in general, girls presented higher prevalence and persistence rates of anxiety than boys (Orgilés, Mendez, Espada, Carballo, & Piqueras, 2012; Van Oort et al., 2009). Taking into account the evolution of the SCARED scores by gender, the results showed that girls obtained higher scores than boys in the third phase, indicating that anxiety in girls may increase with age. Moreover, the results also showed a statistically significant difference in the evolution of the S/P factor scores: in the first phase boys obtained higher scores than girls and in contrast, in the third phase girls scored higher, and this was not consistent with the results of Essau, Anastassiou-Hadjicharalambous, and Muñoz (2012), who found that both younger and older boys obtained lower scores than girls for S/P. As in other studies, gender differences may be explained by a genetic predisposition of girls (Franic et al., 2010).

Another focus of this study was to explore the presence of associated symptoms in children with persistent anxiety. In comparison with those that did not score over the SCARED cut-off point in any phase, significant differences were found for depression, obsessive, bulimia, and vocal tic symptoms. These results are congruent with previous studies which refer to the high rate of co-occurrence of anxiety and depression symptoms in young subjects (Masi et al., 2004; Mathew et al., 2011). Our data were consistent with this in that they also showed that high CDI scores predicted the persistence of anxiety, i.e. depression appears to be associated with the most severe form of anxiety. All of these data support the idea that more research is needed in order to gain a better understanding of the known relationship between anxiety and depression. As for the co-occurrence of anxiety and eating disorder symptoms, our results are also congruent with other studies (Hudson, Hiripi, Pope, &

Kessler, 2007; Hughes, 2012). We thus argue that an early onset anxiety and its persistence could be an important vulnerability factor for the occurrence of associated eating problems. Moreover, the age of the subjects in the last phase of the study coincides with the period in which some authors stated that the possible emotional difficulties and social functioning of the individuals play an important role in the development and maintenance of psychopathological problems (Harrison, Sullivan, Tchanturia, & Treasure, 2010; McLoone, Hudson, & Rapee, 2006; Striegel-Moore & Bulik, 2007). Nevertheless, no relationship between having social impairment and presenting persistent anxiety was found in our study. This could be because the subjects in our sample were younger than in other studies (Burstein et al., 2011; Gren-Landell et al., 2009), or perhaps because the parents were poor informants about their children's social competences, or due to the fact that we analyzed anxiety symptoms instead of anxiety disorders and therefore the symptoms cause less interference. Additionally, the data showed that subjects who presented persistent rates of SA presented the highest rates of co-occurrence, with depression, dysthymia, and obsessive symptoms among others. Children with SA are therefore at risk of presenting other associated anxiety disorders (Kossowsky et al., 2013). Although SA scores decreased over time, the presence of SA at early ages is highly related with its persistence, and when SA persists, the subjects are at risk of presenting other associated symptoms.

This study presents some limitations. One limitation was the use of a self-reporting questionnaire, with the possibility of the responders misunderstanding some questions. However, SCARED demonstrated good properties as an anxiety screening test, and translated versions of the original have been found to be reliable in assessing symptoms in other countries and ethnic groups, and this is true of the recently published Spanish version (Canals et al., 2012). Another limitation was that the study did not control for whether the subjects had been treated in any of the three phases. Also, the fact that the socio-demographic data were only assessed at baseline could also be considered a limitation, as these data may have changed over three years. However, the major limitation was that despite our efforts to ensure maximum participation in the third phase, the rate of attrition was considerable. In order to control the significant differences related to the SES factor between subjects who participated in the final phase and those who did not, all the analyses were adjusted for SES. On the other hand, no differences were found in gender, birthplace, family type, or anxiety and depression.

In conclusion, the results showed that anxiety symptomatology is a persistent phenomenon throughout early adolescence, and that subjects with persistent anxiety presented

high co-occurrence rates. This involved a worsening of the clinical prognosis of these children. Identifying the factors that precede, maintain, or exacerbate the anxiety is therefore essential for early detection and treatment. However, incidence was lower in the last assessment than in the first, suggesting that anxiety symptoms appeared in earlier stages. In fact, it is possible that subjects presenting an incidence of anxiety in the third phase were subjects with previous subclinical levels of anxiety, and that the incidence is probably due to this period coinciding with the onset of adolescence and some subjects may have presented adaptive anxiety. It was also found that in addition to previous anxiety, the subjects' gender and the previous depression symptoms were more closely related to the anxiety's persistence than the anthropometric variables and other socio-demographic variables. Taking all the above into account, we suggest that it is necessary to undertake more prospective follow-up studies on the course of anxiety in clinical and non-clinical populations, to ascertain which factors are related with the chronicity and severity of anxiety, and in order to carry out appropriate interventions.

**Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## 5.4. Estudi dels factors psicopatològics associats amb el rendiment acadèmic durant els primers anys de l'adolescència


**Psychopathological factors associated with academic achievement in early adolescence: A three-year prospective study**

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**Resum:** Els resultats obtinguts mostren que el rendiment acadèmic global dels subjectes que es troben a l'inici de l'adolescència es veu influït per variables com el nivell socioeconòmic, els símptomes depressius, l'ansietat persistent i el TDAH.

Concretament, els símptomes depressius previs són consistentment un factor predictor del rendiment acadèmic en qualsevol matèria. Tanmateix l'ansietat persistent presenta una relació negativa amb el rendiment acadèmic.

En canvi, pel que fa als símptomes d'ansietat generalitzada i de fòbia social, apareixen com un factor positivament relacionat amb el rendiment acadèmic, de manera que els subjectes que manifesten certs nivells d'aquests símptomes mostren un millor rendiment acadèmic. Els subjectes provinents d'entorns socioeconòmics més favorables tendeixen a presentar un millor rendiment acadèmic, i aquest resultat apareix de manera consistent pel que fa al rendiment en matemàtiques.

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
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# Psychopathological factors associated with academic achievement in early adolescence: A three-year prospective study

## ABSTRACT

This three-phase prospective study investigated psychosocial factors predicting or associated with academic achievement. An initial sample of 1,514 school-age children was assessed with screening tools for emotional problems (*Screen for Childhood Anxiety and Related Emotional Disorders; Leyton Obsessional Inventory-Child Version; Children's Depression Inventory*). The following year, 562 subjects (risk group/without risk group) were re-assessed and attention deficit/hyperactivity disorder (ADHD) was assessed. Two years later, 242 subjects were followed, and their parents informed about their academic achievement. Results showed that early depression, persistent anxiety symptoms, and ADHD were predictors of lower academic achievement. However, some anxiety symptoms can improve academic achievement. Socio-economic level (SES) was positively related to academic achievement. We can conclude that in the transition period to adolescence, school-health professionals and teachers need to consider the emotional issues of students to avoid unwanted academic outcomes.

**KEYWORDS:** academic achievement, early adolescence, psychopathology, prospective study

# INTRODUCTION

As Calero, Choi, and Waisgrais pointed out (2010) educational failure is one of the major concerns of the Spanish educational system. These authors defined educational failure as the rate of individuals who do not succeed in finishing the period of compulsory education and who, therefore, do not acquire the basic competences required by the labor market.

In the year 2000, the Organization for Economic Co-operation and Development (OECD) initiated a study that aims to evaluate education systems worldwide by testing the skills and knowledge of 15-year-old students. This study is called the Programme for International Student Assessment (PISA). It is published every three years and is useful for assessing the extent to which students can apply their knowledge to real-life situations at the end of compulsory education. The academic achievement of the Spanish students is below the average of the 34 OECD countries (PISA, 2012). In the year 2009, 25.9% of Spanish children did not obtain the compulsory education certificate (Ministry of Education, Spanish Government). Likewise, the recent study by Fernández-Macías, Antón, Braña, and Muñoz-De Bustillo (2013) showed that the rate of early school leaving in Spain stands at 31.9%, the third highest of the Europe Union countries. This rate might be due to the massive wave of immigration in Spain, because teenagers of immigrant origin have been shown to be considerably more likely to leave school earlier. On the other hand, it was suggested that other factors such as the weaknesses of the vocational system or parent's educational attainment and socio-economic position were also related to the risk of early school leaving. According to these authors, the concept of early school leaving entails leaving the formal school system before completing the period of upper secondary education, and includes the concept of educational failure. In this regard, low levels of academic achievement probably precede educational failure and early school leaving.

The literature describes a wide variety of factors that are directly or indirectly related to academic achievement or which predict its level. Intelligence,

personality and learning or developmental disorders more directly explain educational achievement, but other factors such as gender, parental involvement and educational level, the quality of the teacher-child relationship, the presence of psychopathological symptoms or physical condition are also important (Chamorro-Premuzic & Furnham, 2005; Karbach, Gottschling, Spengler, Hegewald, & Spinath, 2013; Ly, Zhou, Chu, & Chen, 2012; Pérez-Sánchez, Betancort-Montesinos, & Cabrera-Rodríguez, 2013). Considering that early adolescence is a time of important transitions at the physical and psychological level, and that in this period children have to adapt to many changes in academic routines and be more autonomous in managing their work and social life, it is hardly surprising that some of them experience stress, present emotional and social functioning problems and have trouble maintaining academic standards (Barber & Olsen, 2004).

Specifically, low academic achievement has been shown to be associated with both depression and anxiety (Aronen, Vuontela, Steenari, Salmi, & Carlson, 2005; Lundy, Silva, Kaemingk, Goodwin, & Quan, 2010; Marcotte, Lévesque, & Fortin, 2006). In this regard, the results of Quiroga, Janosz, Lyons, and Morin (2012) indicated that depression was a vulnerability factor of low academic attainment that aggravated the risk associated with grade retention although Fergusson and Woodward (2002) suggested that the effect of depression was limited. Authors studying the relation of anxiety symptoms and academic achievement showed that anxiety was negatively correlated with course grades and interferes with working memory (Keogh, Bond, French, Richards, & Davis, 2004; Christopher & MacDonald, 2005). These associations between anxiety and depression symptoms and low academic achievement can be explained by affective, social and cognitive manifestations of the emotional disorders which can result in an inability to concentrate, intrusive thoughts or a disruption of the working memory processes (Ng & Lee, 2010, Christopher & MacDonald, 2005, Visu-Petra, Cheie, Benga, & Packiam-Alloway, 2010).

In addition, most research on adolescents' academic achievement now studies behavioural problems and has found ADHD to be consistently associated

with lower academic achievement. Several authors have found that ADHD involves executive functions' problems, attention disturbances, and behavioural problems which have a negative impact on children's academic outcomes. (Langberg, Dvorsky, & Evans, 2013; Scholtens, Rydell, & Yang-Wallentin, 2013).

In this context, the aim of the present study was to observe whether previous emotional symptoms (depression and anxiety) influence academic achievement in early adolescence. The possible influence of ADHD and socio-demographic factors was also examined. On the basis of the findings of other studies, we hypothesised that academic achievement may be affected by ADHD manifestations, socio-demographic factors, and also anxiety and depression symptoms.

# MATERIAL AND METHODS

## Participants

A total of 2,023 children in grades four (9-10 years old), five (10-11 years old), and six (11-12 years old) of primary school were invited to participate in a three-phase epidemiological study of anxiety and depression disorders. They came from thirteen randomly chosen primary schools (seven state schools and six state-subsidized private schools) in Reus (Spanish town of 100,000 inhabitants).

The baseline sample was a group of 1,514 children (720 boys) (mean-age=10.23; SD=1.23). A total of 39.5% of the children belonged to low SES families, 42.5% to medium SES families and 18% to high SES families. Most of the sample (87.5%) was born in Spain, and 85.9% belonged to a family group consisting of both parents and their children. After this first time (T1) sample had been screened, 562 students (254 boys) (mean-age=11.25; SD=1.04) were selected to participate in the second time (T2) either as subjects at risk of anxiety or depression disorders (N=405; 72.1%) or as members of a control group

without risk (N=157; 27.9%). Two years later all 562 subjects were invited to participate in the third time (T3) follow-up. Of these, 242 subjects (95 boys) (mean-age=13.52; SD=.94) participated. Parents were asked to respond to a questionnaire about their children's academic achievement. A total of 170 questionnaires were returned and are reported in the results section.

No differences were found between the LOI-CV, SCARED and CDI scores of subjects who participated in the third phase and subjects who dropped out of the study. Neither were there any differences between these two groups in terms of socio-demographic variables. However, there were differences related to the SES factor: low SES participants were associated with higher dropout rates than medium or high SES participants (Chi-square$_{2.561}$=13.557; p=.001).

## Measures

***Screen for Childhood Anxiety and Related Emotional Disorders*** (SCARED; Birmaher et al., 1997) is a 41-item self-report questionnaire that assesses anxiety disorder symptoms in children and adolescents aged 8 to 18. Subjects are asked the frequency of each symptom on a 3-point Likert-type scale: 0 (almost never), 1 (sometimes), 2 (often). The reliability of the Spanish version is α=.86, and consists of four factors: somatic/panic, social phobia, generalized anxiety and separation anxiety (Vigil-Colet et al., 2009). A score of 25 was considered to be the cut-off point for risk of anxiety (Birmaher et al., 1997; Canals, Hernández-Martínez, Cosi, & Domènech, 2012a). SCARED was administered in all three phases.

***Children's Depression Inventory*** (CDI; Kovacs, 1992) is a 27-item self-report inventory for assessing depression in subjects aged 7 to 17. Children selected the sentence from each group that best described themselves in the two previous weeks. The reliability of this version has been reported to be good (α=.81 - .85) (Figueras, Amador-Campos, Gómez-Benito, & Del Barrio, 2010) and was shown to be so in the present study (α=.83). A score of 17 was considered to be the cut-

off point for risk of depression (Canals, Martí-Henneberg, Fernández-Ballart, & Domènech, 1995). CDI was administered in T1 and T2.

***Leyton Obsessional Inventory-Child Version*** (LOI-CV; Berg, Whitaker, Davies, Flament, & Rapoport, 1988) is a 20-item self-report questionnaire about the presence ("yes") or absence ("no") of a number of obsessive preoccupations and behaviours. For each positive response, a rating of interference in personal functioning must be indicated (range 0-3, no interference-high interference). The reliability found in the Spanish version was excellent (α=.90) and its validity as a screening test was supported (Canals, Hernández-Martínez, Cosi, Lázaro, & Toro, 2012b). A score of 21 was considered to be the cut-off point for risk of OCD (Canals et al., 2012b). LOI-CV was administered in all phases.

***Youth's Inventory-4*** (YI-4; Gadow & Sprafkin, 1999) is a self-report rating scale that evaluates symptoms of emotional and behavior disorders in adolescents. It contains 120 items that correspond to the symptoms of 18 categories of DSM-IV disorders, and it is a valid tool for assessing symptoms in clinically referred youths (Gadow et al., 2002). In this study, we examined the following symptoms: depression, conduct disorder, eating disorder, tics, schizoid personality, schizophrenia, substance abuse and ADHD. YI-4 was administered in T3 and demonstrated high internal consistency (α=.95).

***Mini-International Neuropsychiatric Interview for Kids*** (M.I.N.I.-Kid; Sheehan et al., 1998) is a structured diagnostic interview for children aged 6 to 17 based on DSM-IV and ICD-10 criteria. It is a short instrument assessing 23 axis I disorders. Interrater and test-retest Kappas were substantial to almost perfect (.64-1) for all individual M.I.N.I.-Kid disorders except dysthymia. Recently, the MINI-Kid has proven its reliability and validity in a sample of outpatients and controls (Sheehan et al., 2010). For this study, we used the ADHD diagnoses and took into account all the ADHD subtypes defined in the DSM-IV-TR (ADHD-

Inattentive [ADHD-I], ADHD-Hyperactive/Impulsive [ADHD-HI], and ADHD-Combined [ADHD-C]). MINI-Kid was administered in T2.

To assess the socio-demographic characteristics of the sample, a ***socio-demographic questionnaire*** designed by the authors of this study was used. Children answered questions about age, gender, place and date of birth, family type and parents' occupation. Parents corroborated this information. The SES was established by the Hollingshead index (Hollingshead, 2011), which determines the social status of individuals taking into account their occupation and their level of education. For this study, family SES was determined by combining data obtained from the father and the mother. The scores range from 0 to 66, and we divided this range into three categories (low, medium and high). We considered scores lower than 22 to be low, scores between 23 and 44 to be medium, and scores over 44 to be high. This questionnaire was administered in T1.

***Academic achievement*** was assessed by asking parents about the academic achievement of their children in language, social sciences, mathematics, and natural sciences. There were four items with four response possibilities: 1 (fail; 0-3), 2 (below average; 4), 3 (average; 5-6) and 4 (above average; 7-10). Apart from the achievement in each subject, we have defined the overall academic achievement variable using the sum of the scores in language, social sciences, mathematics, and natural sciences.

## Procedure

Before we began the study, the project was approved by the Rovira i Virgili University ethics committee, and was given permission by the Ministry of Education of the Catalan Government. Then, a representative sample of subjects was selected, and cluster sampling was conducted by randomly selecting a set of thirteen primary schools from a total of 26 schools from all five representative areas of Reus. Then, the school boards were contacted, all of whom agreed to

participate. Subsequently, a letter was sent to all parents informing them of the study and asking for their written informed consent.

The first phase took place during the 2006/2007 academic year using a representative sample of school-age subjects in primary grades four (9-10 years old), five (10-11 years old), and six (11-12 years old). The selected participants were followed for two consecutive years (T1 and T2) and, after a one-year break, for another year (T3). In the first phase participants answered screening tests for anxiety (SCARED), obsessive-compulsive symptoms (LOI-CV) and depression (CDI). Socio-demographic data was also collected. Over the following academic year, a subsample was selected of subjects who, according to their cut-off scores in the screening tests (SCARED, CDI and/or LOI-CV), were at risk of mood and anxiety disorders. Additionally, controls with the same age and gender characteristics, but without risk scores on any test, were selected. In T2, SCARED, LOI-CV and CDI were re-administered to participants. Psychological disorders were assessed using the M.I.N.I.-Kid. Finally, in the third time, all the subjects from the second time were re-invited to participate and a retest with SCARED and LOI-CV was conducted. The YI-4 was also administered in order to evaluate psychopathology. The parent-reported academic performance defined our variable of academic achievement. The research participants completed the questionnaires in small groups of three or four and the researchers were present to instruct the children on how to answer the surveys or resolve doubts.

**Statistical analysis**

Multiple linear regression models were performed to identify predictors and variables related to overall academic achievement, and to achievement in language, social sciences, mathematics, and natural sciences using SPSS 20.0. Three regression models were performed for each dependent variable. The variables selected and entered into each model using the ENTER method were the following:

In *step* 1 the variables collected at Time 1 (T1) were entered: SCARED factor scores, LOI-CV total scores, CDI total scores, and socio-demographic variables (birthplace, family type, age and gender). The model was adjusted for SES.

Step 2, to the variables in step 1 we added: the persistence-at-one-year variables. These variables were created using the first phase risk scores on the SCARED or CDI or LOI-CV and also the risk scores of the second phase. In this model the socio-demographic variables were also entered. The model was adjusted for SES and for ADHD diagnoses.

To observe possible associations between T3 variables and academic achievement, in step 3 a cross-sectional model was performed and the following scores were entered: SCARED factor scores, LOI-CV total scores, and YI-4 scores. Socio-demographic variables were also added. The model was adjusted for SES.

Collinearity between all the selected variables was assessed by computing Pearson correlations and analyses showed that the SCARED total score was collinear with the SCARED factor scores. For this reason, the SCARED factor scores were selected instead of the total score. No collinearity was found between depressive and anxiety symptoms, or between depressive and ADHD symptoms.

## RESULTS

Descriptive data of academic achievement showed a mean of 13.05 (SD=2.79) for overall academic achievement. For the other academic subjects data showed: language mean=3.23 (SD=.81); social sciences mean=3.26 (SD=.88); mathematics mean=3.19 (SD=.86), and natural sciences mean=3.36 (SD=.79).

The multiple linear regression models were performed for overall academic achievement, and for academic achievement in each school subject (see Table 1).

The results show that in step 1 (T1) the best predictors were SES and the CDI total scores for overall academic achievement, mathematics, and natural and social sciences. Lower depression symptoms at T1 predicted higher academic achievement at T3, while higher SES levels predicted higher academic achievement at T3. The models explained 10.5% of the overall academic achievement ($F_{11.163}$=2.740, p=.003), and 5.6%, 9.1%, and 11.4% of the academic achievement in social sciences ($F_{11.166}$=1.889, p=.045), mathematics ($F_{11.166}$=2.515, p=.006), and natural sciences ($F_{11.164}$=2.922, p=.002), respectively. In step 2 (T1 + T2) the predictors that were significant for both overall academic achievement and mathematics achievement were SES, T1 CDI, SCARED persistence, T2 social phobia, and ADHD-C. Moreover, results showed that T1 CDI was a consistent and significant predictor of all academic achievement. In spite of the negative influence of the persistence of anxiety on academic achievement, data showed that higher social phobia symptoms at T2 predicted higher overall academic achievement, and achievement in language and mathematics. Also, higher generalized anxiety symptoms at T2 were related to greater achievement in natural sciences. The models explained 37.1% of overall academic achievement ($F_{21.125}$=4.510, p<.001), and 27.2%, 23.9%, 19.4%, and 30.7% of the academic achievement in language ($F_{21.126}$=3.241, p<.001), social sciences ($F_{21.127}$=2.904, p<.001), mathematics ($F_{21.127}$=2.460, p=.001), and natural sciences ($F_{21.126}$=3.660, p<.001), respectively.

Throughout step 3, results showed associations academic achievements and T3 generalized anxiety, T3 separation anxiety, and ADHD symptomatology. Higher levels of generalized anxiety symptoms at T3 were related to higher academic achievement at T3, and lower separation anxiety symptoms at T3 were related to higher academic achievement at T3. In this regard, results showed that lower ADHD symptoms at T3 were associated with higher academic achievement. Results also showed a significant influence of SES on mathematics achievement. The statistically significant models explained 18.1% of overall academic achievement ($F_{18.164}$=3.010, p<.001), and 14.3%, 17.7%, and 13.7% of

the academic achievement in language ($F_{18.166}$=2.541, p=.001), social sciences ($F_{18.167}$=3.002, p<.001), and mathematics ($F_{18.167}$=2.478, p=.001), respectively.

## DISCUSSION

Given that the rates of educational failure in Spain are high, the purpose of this three-phase prospective study was to assess whether previous emotional disturbances apart from ADHD and socio-demographic variables could influence academic achievement in a developmental transition stage such as the beginning of adolescence. In this regard, it is known that problems of academic achievement are one of the most robust predictors of school dropout (Newcomb et al., 2002) and are therefore also predictors of educational failure. In our sample, the academic achievement showed mean scores around 5-6, supporting a low performance in comparison with other European countries (PISA, 2012).

Overall, results showed that emotional variables play an important role in academic achievement. In fact, these variables presented a stronger relationship with academic achievement than socio-demographic ones, because no conclusive results were found for gender, age, family type and birthplace. Results were only statistically significant for SES and showed that it was a positive predictor of overall academic achievement and achievement in the different school subjects. These findings support a great deal of other research that has found evidence of a positive relationship between a high family SES and high academic achievement (Srin, 2005). This may be because the parents of children from high SES environments probably have high levels of education and higher occupational prestige. Therefore, they may value education more, or they might be more demanding with their children, better equipped to help them with school work, more at ease in the school setting or more encouraging. Moreover, as in the present study, Caro, McDonald, and Willms (2009) found that there is a difference in mathematics achievement between students of higher and lower SES, and that this difference is more significant in early adolescence. In

agreement with Caro et al. (2009), we suggest that it is likely that educational disparities associated with SES tend to increase as students advance in school. In this regard, Hackman, Farah, and Meaney (2010) suggested that programs and policies should attempt to alleviate disparities in SES and improve the mental health and academic achievement of children. As in other studies of emotional variables from other countries (Fröjd et al., 2008), the present results have shown that previous depressive symptomatology is a consistent and statistically significant predictor of poor academic results. It may be negatively correlated with academic achievement because the symptoms of apathy, trouble concentrating, anhedonia, irritability or sadness can lead to a reduction in the cognitive resources available, deficits in working memory, and a reduction in motivational mechanisms (Matthews, Coghill, & Rhodes, 2008; Valiente, Swanson, & Eisenberg, 2012). Results have also shown that the persistence of anxiety throughout development has a negative influence on academic achievement. This type of symptom can be chronic and cause such important problems as absenteeism or poor academic achievement (Rapee, Schniering & Hudson, 2009). For example, somatic anxiety symptoms can be quite severe and may lead to children missing more school or having trouble paying attention during class (Hughes, Lourea-Waddell, & Kendall, 2008), thus affecting academic achievement. As found by Gills-Taquechel, Fletcher, Vaughn, Denton, and Taylor (2013), results also show that separation anxiety present an inverse relation with academic achievement. We suggest that separation anxiety is an important factor because the third phase coincides with a transition for most of the participants (onset of adolescence), and it is possible that at this moment subjects assess their attachment with their parents. Early adolescents probably need to feel secure, and if they do not they may become vulnerable to developing anxiety disorders (Esbjorn, Bender, Reinholdt-Dunne, Munck, & Ollendick, 2012). Furthermore, although obsessive-compulsive symptomatology can also cause problems in the school context (Geller & March, 2012) our results were not conclusive. This could be due to the fact that obsessive-compulsive and anxiety symptoms frequently co-occur (Langley, Lewin, Bergman, Lee, & Piacentini,

2010). In contrast, it has been found that anxiety has not always proved to have a negative influence on academic achievement. Our results show that generalized anxiety and social phobia symptoms present a positive relation with academic achievement. Therefore, generalized anxiety may produce moderate levels of alertness and tension in students, thus leading to better achievement in tasks that require a lot of attention. These students may also be so concerned about their studies that they spend more time on them than on any other aspect of their lives. Generalized anxiety may also compensate for such other symptoms as conduct disorder manifestations. Social phobia symptomatology may produce high levels of motivation to avoid possible negative opinions from their classmates. In this vein, recent results have suggested that students with good working memory and higher levels of anxiety achieved more than other individuals (Owens, Stevenson, Hadwin & Norgate, 2014). The results of Owens et al. (2014) extend those of Eysenck and Derakshan (2011), who found that highly anxious individuals will be motivated to do their tasks well to avoid negative evaluations. Therefore, subjects with high levels of anxiety and a high working memory capacity have the resources to manage their motivation properly and to achieve more academically. There may be individual differences between those with and without the wherewithal to cope with intrusive thoughts of a negative reaction to failure, such as working memory capacity.

Our data support the hypothesis that the presence of ADHD is related to worse academic achievement, as has been shown in recent studies (Scholtens et al., 2013).

According to the present results, emotional and behavioral problems at school may need to be detected if low levels of academic achievement are to be prevented. Psychologists should also consider integrating complete mental health education and learning coping strategies in the curriculum (Mychailyszyn, Brodman, Read, & Kendall, 2012). Subjects whose academic achievement is low, then, may need possible risk factors to be controlled and preventive intervention to be implemented if unwanted long-term outcomes are to be prevented. The prevention of anxiety and depression, and early intervention programs in schools

(for example, cognitive behavioural therapy [CBT] programs) should be encouraged because they can lead to significant improvements in behaviour at school and home, self-control, social skills and self-esteem (Neil & Christensen, 2009; Yeo & Choi, 2011). Although Durlak, Weissberg, Dymnicki, Taylor, and Schellinger (2011) suggested that programs that promote learning of social and emotional competences are associated with greater well-being and better academic achievement, other findings (Stallard et al., 2012) indicate that classroom-based prevention programs for reducing symptoms of depression may not be effective. Therefore, future research on possible school intervention is needed.

The importance of our findings must be evaluated in the light of some limitations. Firstly, the follow-up sample was small. Despite the efforts we made to ensure the maximum participation possible in the third phase, the study suffered from reduced parental consent and few parents returned the completed questionnaires. Secondly, we had no information on the specific learning disorders or intelligence quotient (IQ) of the children. High or low IQ may have a direct effect on learning ability. Thus, a lower IQ or specific learning disabilities may have an emotional effect on individuals when they see that they cannot do what others can. We have only been able to adjust the analyses for ADHD. Thirdly, the socio-demographic data were only collected at baseline and these data may have changed over the three years. And finally academic achievement was assessed using the information provided by parents, and it may have been better to use the ratings provided by teachers. Despite these limitations, the study extends our knowledge of the possible causes of the high rates of educational failure that exist in Spain.

In summary, the data show that symptoms of early depression and the persistence of anxiety were closely related to academic difficulties in early adolescence. On the other hand, moderate levels of generalized anxiety and social phobia may be related to responsibility and academic motivation. As has been shown in recent studies, ADHD symptoms interfere considerably in children's academic life. However, with the exception of SES, no conclusions could be drawn about socio-

demographic variables. Finally, we suggest that during the transition period to adolescence it is important to detect emotional problems, in addition to behavioral and learning problems for the prevention of academic difficulties. In the future, more longitudinal studies are needed.

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**Table 1** Predictors and variables related to overall academic achievement and academic achievement for each school subject

| | Overall academic achievement | | | | Language academic achievement | | | |
|---|---|---|---|---|---|---|---|---|
| | ***B*** | ***t*** | ***p*** | ***Model*** | ***B*** | ***t*** | ***p*** | ***Model*** |
| **Step 1 (T1)** | | | | | | | | |
| SES | .293 | 2.712 | .007 | $R_c^2$*100=10.5 | - | - | - | $R_c^2$*100=5 |
| T1 CDI | -.130 | -3.503 | .001 | $F_{11.163}$=2.740 | -.028 | -2.547 | .012 | $F_{11.165}$=1.793 |
| | | | | $p$=.003 | | | | $p$=.059 |
| **Step 2 (T1 + T2)** | | | | | | | | |
| SES | .324 | 2.954 | .004 | $R_c^2$*100=37.1 | - | - | - | $R_c^2$*100=27.2 |
| T1 CDI | -.187 | -4.841 | <.001 | $F_{21.125}$=4.510 | -.049 | -4.195 | <.001 | $F_{21.126}$=3.241 |
| SCARED persistence at one year | -1.721 | -2.413 | .018 | $p$<.001 | - | - | - | $p$<.001 |
| T2 Social phobia SCARED factor | .216 | 2.398 | .018 | | .080 | 2.888 | .005 | |
| T2 Generalized anxiety SCARED factor | - | - | - | | - | - | - | |
| ADHD-C | -3.415 | -2.868 | .005 | | - | - | - | |
| **Step 3 (T3)** | | | | | | | | |
| SES | - | - | - | $R_c^2$*100=18.1 | - | - | - | $R_c^2$*100=14.3 |
| T3 Generalized anxiety SCARED factor | .313 | 4.135 | <.001 | $F_{18.164}$=3.010 | .074 | 3.368 | .001 | $F_{18.166}$=2.541 |
| T3 Separation anxiety SCARED factor | -.189 | -2.190 | .030 | $p$<.001 | - | - | - | $p$=.001 |
| YI-4 ADHD | -.094 | -2.571 | .011 | | -.026 | -2.472 | .015 | |

Level of statistical significance $p < .05$.

Selected variables to enter into step 1: T1 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T1 LOI-CV (total score); T1 CDI (total score); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES.

Selected variables to enter into step 2: T1 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T1 LOI-CV (total score); T1 CDI (total score); T2 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; persistence-at-one-year variables→ SCARED (1: persistence; 0: no persistence), CDI (1: persistence; 0: no persistence), and LOI-CV (1: persistence; 0: no persistence); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES and for ADHD diagnoses (ADHD-I, ADHD-HI, ADHD-C).

Selected variables to enter into step 3: T3 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T3 LOI-CV (total score); YI-4 categories (total scores); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES.

**Table 1.** Predictors and variables related to overall academic achievement and academic achievement for each school subject **(cont.)**

| | Social sciences academic achievement | | | | Mathematics academic achievement | | | | Natural sciences academic achievement | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***B*** | ***t*** | ***p*** | ***Model*** | ***B*** | ***t*** | ***p*** | ***Model*** | ***B*** | ***t*** | ***p*** | ***Model*** |
| **Step 1 (T1)** | | | | | | | | | | | | |
| SES | .082 | 2.389 | .018 | $R_c^2$*100=5.6 | .104 | 3.231 | .002 | $R_c^2$*100=9.1 | .063 | 2.108 | .037 | $R_c^2$*100=11.4 |
| T1 CDI | -.028 | -2.395 | .018 | $F_{11.166}$=1.889 | -.028 | -2.503 | .013 | $F_{11.166}$=2.515 | -.043 | -4.154 | <.001 | $F_{11.164}$=2.922 |
| | | | | $p$=.045 | | | | $p$=.006 | | | | $p$=.002 |
| **Step 2 (T1 + T2)** | | | | | | | | | | | | |
| SES | .100 | 2.824 | .006 | $R_c^2$*100=23.9 | .086 | 2.266 | .025 | $R_c^2$*100=19.4 | - | - | - | $R_c^2$*100=30.7 |
| T1 CDI | -.041 | -3.288 | .001 | $F_{21.127}$=2.904 | -.032 | -2.422 | .017 | $F_{21.127}$=2.460 | -.057 | -4.840 | <.001 | $F_{21.126}$=3.660 |
| SCARED persistence at one year | - | - | - | $p$<.001 | -.675 | -2.697 | .008 | $p$=.001 | -.503 | -2.310 | .023 | $p$<.001 |
| T2 Social phobia SCARED factor | - | - | - | | .073 | 2.287 | .024 | | - | - | - | |
| T2 Generalized anxiety SCARED factor | - | - | - | | - | - | - | | .068 | 2.545 | .012 | |
| ADHD-C | -.774 | -2.137 | .035 | | -.795 | -2.051 | .043 | | -.825 | -2.444 | .016 | |
| **Step 3 (T3)** | | | | | | | | | | | | |
| SES | - | - | - | $R_c^2$*100=17.7 | .081 | 2.513 | .013 | $R_c^2$*100=13.7 | - | - | - | $R_c^2$*100=5.8 |
| T3 Generalized anxiety SCARED factor | .102 | 4.316 | <.001 | $F_{18.167}$=3.002 | .065 | 2.788 | .006 | $F_{18.167}$=2.478 | .071 | 3.076 | .003 | $F_{18.165}$=1.567 |
| T3 Separation anxiety SCARED factor | -.067 | -2.489 | .014 | $p$<.001 | - | - | - | $p$=.001 | - | - | - | $p$=.076 |
| YI-4 ADHD | -.028 | -2.471 | .015 | | - | - | - | | - | - | - | |

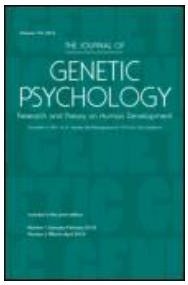
Level of statistical significance $p < .05$.

Selected variables to enter into step 1: T1 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T1 LOI-CV (total score); T1 CDI (total score); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES.

Selected variables to enter into step 2: T1 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T1 LOI-CV (total score); T1 CDI (total score); T2 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; persistence-at-one-year variables→ SCARED (1: persistence; 0: no persistence), CDI (1: persistence; 0: no persistence), and LOI-CV (1: persistence; 0: no persistence); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES and for ADHD diagnoses (ADHD-I, ADHD-HI, ADHD-C).

Selected variables to enter into step 3: T3 SCARED factor scores→ somatic/panic, social phobia, generalized anxiety, separation anxiety; T3 LOI-CV (total score); YI-4 categories (total scores); family type (0: single parent; 1: nuclear); birthplace (0: foreign; 1: native); age (years); and gender (1: boy; 2: girl). The model was adjusted for SES.

## 5.5. Estudi de l'associació entre el polimorfisme del gen MAOA (MAOA-uVNTR) amb l'ansietat autoinformada i d'altres símptomes psicopatològics en una mostra comunitària d'adolescents




**Association study of Monoamine Oxidase-A gene promoter polymorphism (MAOA-uVNTR) with self-reported anxiety and other psychopathological symptoms: Study in a community sample of early adolescents**

Núria Voltas, Estefania Aparicio, Victoria Arija, Josefa Canals

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**Sotmès a la revista**

**Resum:** Els resultats mostren que les noies amb una una alta activitat del polimorfisme del gen MAOA presenten una major quantitat de símptomes d'ansietat total i d'ansietat generalitzada, que les noies amb una baixa activitat del polimorfisme. En el cas dels nois, els que presenten una baixa activitat del polimorfisme del gen MAOA, presenten una major quantitat de símptomes de fòbia social que els que presenten una baixa activitat del polimorfisme. Els resultats pel que fa als símptomes conductuals no mostren relacions significatives entre els al·lels del polimorfisme del gen MAOA i la presència d'aquests símptomes. En el cas del sexe femení els resultats mostren que també existeix una influència de variables ambientals com els esdeveniments vitals estressants.

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# Association study of Monoamine Oxidase-A gene promoter polymorphism (MAOA-uVNTR) with self-reported anxiety and other psychopathological symptoms in a community sample of early adolescents

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|---|---|
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| | |

# Association study of Monoamine Oxidase-A gene promoter polymorphism (MAOA-uVNTR) with self-reported anxiety and other psychopathological symptoms in a community sample of early adolescents

## Abstract

The polymorphism upstream of the gene for monoamine oxidase A (MAOA-uVNTR) is reported to be an important enzyme involved in human physiology and behavior. With a sample of 228 early adolescents from a community sample (143 girls and 85 boys), we examined the influence of environmental variables and MAOA-uVNTR alleles on the scores obtained in the *Screen for Childhood Anxiety and Related Emotional Disorders* and in the *Child Symptom Inventory-4*. Our results showed that girls with the high-activity MAOA allele had higher scores for generalized and total anxiety than their low-activity peers, whereas boys with the low-activity allele had higher social phobia scores than boys with the high-activity allele. Results for conduct disorder symptoms did not show a significant relationship between the MAOA alleles and the presence of these symptoms. Our findings support a possible association between the MAOA-uVNTR polymorphism and psychopathological disorders such as anxiety, which affects high rates of children and adolescents.

**Keywords** MAOA-uVNTR, gender, anxiety, psychopathology, adolescents

## Introduction

The monoamine oxidase A (MAOA) gene possesses a variable number of tandem repeats polymorphism (MAOA-uVNTR). This polymorphism gives rise to five different alleles depending on whether there are 2, 3, 3.5, 4, or 5 copies of a sequence of 30 base pairs. The alleles have been divided into two groups according to their transcriptional activity, resulting in genotypes with low-activity (MAOA-L) and high-activity (MAOA-H) alleles (Guo, Ou, Roettger, & Shih, 2008; Sabol, Hu, & Hamer, 1998). It has long been documented that the MAOA-uVNTR polymorphism affects the MAOA gene at the transcriptional level and it has been suggested that the polymorphism is involved with diverse mental health conditions in children and adults, including major depressive disorder (Lung, Tzeng, Huang, & Lee, 2011; Rivera et al., 2009), autism spectrum disorders (Tassone et al., 2011; Verma et al., 2014), aggressive behaviors (Byrd & Manuck, 2014), panic disorder (Reif et al., 2012) and attention deficit hyperactivity disorder (ADHD) (Guan et al., 2009; Nymberg et al., 2013). This relationship between allelic variants of the MAOA-uVNTR polymorphism and a particular pattern of psychopathological symptoms was supported by previous studies both in humans and in mice (Cases et al., 1995; McDermott, Tingley, Cowden, Frazzetto, & Johnson, 2009). In this vein, it is known that MAOA is an enzyme that metabolizes neurotransmitters such as dopamine, serotonin, and norepinephrine (Jacob et al., 2005; Shih, Chen, & Ridd, 1999) which are linked to some of the abovementioned

psychopathological problems. Specifically, a large body of research has confirmed the crucial role of the serotonergic and dopaminergic neurotransmission systems in the pathophysiology of emotional and behavioral disorders (Gutiérrez et al., 2004; Marceau & Neiderhiser, 2013; Maron, Nutt, & Shlik, 2012). MAOA is also considered a likely depression and anxiety candidate gene because it is also known that MAO inhibitors have been found to be effective in treating these disorders (Libert et al., 2011; Murphy, Mitchell, & Potter, 1995).

However, studies examining the main effects of MAOA variants for the psychopathological disorders of children and adolescents are relatively few (Lavigne et al., 2013) and, in addition, results are mixed. Although some studies found that MAOA-L was associated with increased conduct disorder (Foley et al., 2004; Prom-Wormley et al., 2009), others found no effects of MAOA variants on conduct problems (Huizinga et al., 2006; Widom & Brzustowicz, 2006). With regard to depression, research on the possible association with MAOA-uVNTR has also been inconclusive: whereas numerous findings implicate low-expression alleles (Cicchetti, Rogosch, Sturge-Apple, 2007; Lavigne et al., 2013, Priess-Groben & Hyde, 2013) others have failed to find any association (Eley et al., 2004) or have found many differences between genders.

In addition, some studies have suggested that the relationship between MAOA variants and certain behaviors can usually be modulated by environmental factors (Caspi et al., 2002; Lavigne et al., 2011; Winham & Biernacka, 2013). Specifically, candidate gene

x environmental interaction (G x E) studies tested the hypothesis that the effect of some environmental variable on some outcome measure (e.g. psychopathological disorders the subjects may present) depends on a particular genetic polymorphism (Keller, 2014). On the other hand, Keller (2014) warns that this type of study (G x E) does not properly control for confounding variables and skepticism has increased about the validity of many of these findings (Duncan & Keller, 2011; Munafo & Flint, 2009). Moreover, it is known that the vast majority of phenotypes are polygenic, which means that they are influenced by multiple genes (Fowler et al., 2009; Plomin, 2008). In addition to genetic and environment interaction, the influence of certain polymorphism may vary depending on gender. In fact, in the case of the MAOA-uVNTR polymorphism there is a certain imbalance between girls and boys because boys have only one X chromosome and MAOA is linked to it.

One of the most accepted hypotheses is the "worrier- versus warrior-gene" hypothesis. This dichotomy refers to the results of previous studies and is related to the fact that aggressive behaviors and impulsivity are associated with male subjects with MAOA-L, whereas anxious behavior is associated with MAOA-H female subjects (Huang et al., 2004; McDermott et al., 2009; Reif et al., 2012; Rivera et al., 2009). In line with this, it is known that emotional and behavioral disorders are highly prevalent, cause severe disturbances, and present a long-term course in children and adolescents from the community (Coughlan et al., 2014; Magiati et al., 2013; Merikangas et al., 2010a,b). For this reason, study of the

biological basis of these disorders could be useful for determining whether psychopathological disorders during early adolescence depend not only on environmental factors but also on biological ones.

Assuming the "worrier- versus warrior-gene" hypothesis, and in light of the uncertainty emerging from the published research, in this study we analyze, by gender, the possible association of MAOA-uVNTR polymorphism alleles with different self-reported anxiety subtypes and other psychopathological symptoms in a sample of early adolescents from the community. We hypothesized that MAOA-uVNTR influence the presence of psychopathological symptoms in the age period studied and that this influence probably depends on gender.

## Methods

### Participants

A total of 245 subjects (147 girls and 98 boys; mean age=13.5; SD=.9) agreed to participate in the third phase of a prospective three-phase longitudinal study and their parents provided written informed consent. More data about the study design and participants have been reported in more detail elsewhere (Voltas, Hernández-Martínez, Arija, Aparicio, & Canals, in press). Of the 245 subjects that agreed to participate in the third phase, 13 were eliminated for presenting incomplete data and four were eliminated as outliers. The final sample therefore comprised 228 subjects (143 girls and 85

boys). The socio-demographic characteristics of the sample are shown in Table 1.

## Measures

The *Child Symptom Inventory* (Gadow & Sprafkin, 1998) is a screening instrument based on DSM-IV criteria. The parent version used in this study contains 97 items classified into 10 categories with a 4-point Likert response format. The CSI-4 has been demonstrated to be valid (Sprafkin, Gadow, Salisbury, Schneider, & Loney, 2002) and its Spanish version has shown excellent internal consistency (Cronbach's $\alpha$ =.99) (Angulo-Rincón et al., 2010). For this study we used all the categories except enuresis and encopresis, motor tics and vocal tics, schizophrenia, and autistic and Asperger symptoms. We created quantitative variables resulting from the sum of the items in each category. Then we created the following two variables: *any disruptive disorder*, which comprised all the ADHD categories, oppositional defiant disorder symptoms, and conduct disorder symptoms; and *any emotional disorder*, which comprised the categories related to anxiety, obsessive-compulsive disorder, and depressive disorder symptoms.

The *Screen for Childhood Anxiety and Related Emotional Disorders* (Birmaher et al., 1997) is a 41-item self-report questionnaire that assesses anxiety disorder symptoms in children and adolescents from 8 to 18 years old. Subjects are asked about the frequency of each symptom using a 3-point Likert response format:

0 (almost never), 1 (sometimes), and 2 (often). The reliability of the Spanish version is α=.86. It consists of four factors called somatic/panic (12 items; α =.78), social phobia (7 items; α=.69), generalized anxiety (9 items; α=.69), and separation anxiety (13 items, α=.70) (Vigil-Colet et al., 2009). A score of 25 has been considered the cut-off point for risk of anxiety (Birmaher et al., 1997; Canals, Hernández-Martínez, Cosi, & Domènech, 2012). Canals et al. (2012) also proposed cut-off scores for the SCARED factors with sensitivities between 74% and 78%. The SCARED was administered in all phases of the study.

*Stressful life events (SLE)* were assessed in the third phase using 10 of the 31 items of the *Adolescent Life Change Event Scale* (Yeaworth, York, Hussey, Ingle, & Goodwin, 1980). First, using a 5-point Likert response format (1 non-affected – 5 highly affected), the participants indicated how they would be affected if they were in each of the proposed situations. Then they indicated which of the situations had happened to them in the previous year. We created a quantitative variable by multiplying each situation experienced by the subject in the previous year by the degree of impact they had marked on the Likert scale for the same situation. The final quantitative variable was the sum of all the situations experienced taking into account the degree of impact attributed by the subject. Cronbach's alpha was .79.

*Academic achievement* was assessed by asking parents about the academic achievement of their children in language, social sciences, mathematics, and natural sciences. There were four items with four

possible responses: 1 (fail), 2 (below average), 3 (average), and 4 (above average). We defined a quantitative variable to represent overall academic achievement using the sum of the scores in language, social sciences, mathematics, and natural sciences.

*Socio-demographic characteristics* of the sample were collected at baseline using a questionnaire designed for this study by the authors. The children answered questions about age, gender, place of birth, date of birth, type of family, and parents' occupations. This information was corroborated by the parents. The socioeconomic status (SES) was established by the Hollingshead index (2011). This index allows the social status of each individual to be determined by categorizing his or her occupation into one of nine categories (from unskilled work to highly skilled work) and his or her level of education into one of seven categories (from non-completed primary education to completed higher education). The status score is estimated by multiplying the occupation scale value by a weight of five and the education scale value by a weight of three and then combining the two scores. We thus determined family SES on a scale from 0 to 66. This gave us three categories (low, medium and high). We considered scores under 22 to be low, scores of between 23 and 44 to be medium, and scores over 44 to be high.

## Genotyping

Genomic DNA was extracted from buccal cells derived from Oragene·DNA self-collection kits (DNA, Genotek). The

polymorphism 30bp VNTR in the promoter of the MAOA gene was genotyped using a previously published protocol (Haberstick et al., 2005). Briefly, polymerase chain reaction (PCR) was performed in a total volume of 20µl containing 20ng of DNA, using the primers forward, 5'–D2–ACAGCCTGACCGTGGAGAAG–3' and reverse, 5'-GAACGGACGCTCCATTCGGA. PCR products included five possible fragment sizes— 291, 321, 336, 351, and 381bp (2, 3, 3.5, 4 and 5 repeats, respectively)—and were classified into two groups. The first group combined those with the 2-repeat and 3-repeat alleles and is subsequently referred to as the low-activity group of the MAOA (MAOA-L). The second group combined those with the 3.5-repeat, the 4-repeat, and the 5-repeat and is subsequently referred to as the high-activity group of the MAOA (MAOA-H).

The MAOA gene is located on the X chromosome; therefore, a heterogeneous genotype does not exist in men. We classified the heterogeneous genotype (i.e. 2/3.5, 2/4, 2/5, 3/4, 3/5, 3.5/4, 3.5/5, 4/5) of girls into the high-activity group, as in other studies (Reif et al., 2012). All trials were repeated twice. If the results were negative or discordant, the trials were repeated 3, 4, or 5 times. Nine subjects were unsuccessfully genotyped for the MAOA gene and were dropped from all genetic analyses.

## Procedure

This study is part of a longitudinal study. For the analyses in this paper we have used data from the third phase.

Before the beginning of the study, the project was approved by the Rovira i Virgili University ethics committee for research on individuals and by the Department of Education of the Government of Catalonia. A representative sample of subjects was then selected, and cluster sampling was conducted by randomly selecting a set of thirteen primary schools (7 state schools and 6 state-subsidized private schools) from a total of 26 schools from all five representative areas of Reus (Catalonia, Spain). We then contacted the school boards and all agreed to participate. After that, a letter was sent to all parents to inform them about the study and to ask for their written informed consent. We then conducted the study in three phases. In the third phase, the children answered the SCARED questionnaire as well as items about the presence of SLE. A saliva sample was also collected from them from which the DNA was extracted for the subsequent analyses of the MAOA-uVNTR polymorphism. The parents answered the CSI-4 questionnaire and the questions about their children's academic achievement. The participants completed the questionnaires in groups of three or four. Researchers were present to instruct the children on how to answer the surveys and use the saliva kits, and to answer any queries.

## Statistical analyses

For statistical analysis we used SPSS software, version 20.0 for Windows.

First the data were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests.

Descriptive data of the socio-demographic and psychopathological characteristics of the sample were presented. Values were expressed as the mean and standard deviation for the quantitative variables, and as percentages for the qualitative variables. Student's t-test and chi-square analyses were used to find any significant differences between boys and girls (see Table 1).

We then fitted multiple linear regression models using the enter method to explore the effect of MAOA-uVNTR polymorphism and other variables (gender, age, SLE, SES, and academic performance) on the presence of anxiety and other psychopathological symptoms. Multiple linear regression models were calculated for boys and girls separately because in previous exploratory analyses we observed an interaction effect between gender and MAOA-uVNTR polymorphism.

Student's t-test analyses were also conducted to examine possible differences between the two genotype subgroups (MAOA-L and MAOA-H) in the SCARED and CSI-4 scores. These analyses were also done separately for each gender.

The Hardy-Weinberg equilibrium (HWE) of the genotype distributions of the girls was approximated for all samples using chi-squared tests. Because of hemizygosity in the male subjects, HWE could not be calculated for them.

Criterion for statistical significance was set at .05 such as other studies (Ducci et al., 2006; Roohi, DeVincent, Hatchwell, & Gadow, 2009).

## Results

As the Kolmogorov-Smirnov and Shapiro-Wilk tests were not significant in any case, the sample distribution was assumed to be normal.

Table 1 shows the socio-demographic and psychopathological characteristics of the sample. Table 2 shows the MAOA-uVNTR alleles and genotype distributions. In girls, allele frequencies were within the Hardy-Weinberg equilibrium ($\chi^2$=2.127; $p$=.345). Due to hemizygosity in male subjects, the Hardy-Weinberg equilibrium could not be calculated for boys.

As the multiple linear regression models showed that overall gender was a significant variable, we performed the models for each gender. T-test analyses were therefore also performed by gender.

The regression models for anxiety were significant for girls. However, the MAOA-uVNTR polymorphism only presented a significant association with the generalized anxiety factor scores (see table 3). SLE was a significant factor related to any anxiety score. Multiple linear regression analyses showed no significant relationships for the scores on the CSI-4 for boys or girls.

Student t-test analyses (see Table 4) showed that MAOA-L boys had higher social phobia factor scores than MAOA-H (MAOA-H group: *M*=4.7, SD=3.2; MAOA-L group: *M*=6.4, SD=3.3; *t*=2.271; *p*=.026). These results were in the opposite direction to the data found for the other anxiety subtypes. SCARED factor scores for both genders were higher in somatic/panic, generalized anxiety and separation anxiety for MAOA-H subjects than for MAOA-L subjects but these results were not statistically significant. Taking this trend into account and to prevent the scores of the social phobia items from attenuating the SCARED total scores, we calculated SCARED total using somatic/panic, generalized anxiety, and separation anxiety factor scores. MAOA-H girls obtained higher SCARED total scores than MAOA-L girls and these results were statistically significant (MAOA-H group: *M*=16.2, SD=8.8; MAOA-L group: *M*=13.5, SD=4.7; *t*=-2.033, *p*=.048). The analyses of the CSI-4 scores did not show statistically significant results.

## Discussion

Overall, in this sample of early adolescents, our results showed significant associations between the variants of the MAOA-uVNTR and the presence of anxiety symptoms. The results also showed different trends between girls and boys.

In agreement with the “worrier- versus warrior-gene” hypothesis, our data showed that high-activity variants of the MAOA-uVNTR polymorphism were associated with anxiety symptoms in girls, as

was found in adult samples (Rivera et al., 2009; Yu et al., 2005) especially for the generalized anxiety factor and for the SCARED total scores. In this regard, at the biological level it is known that high MAOA activity degrades the serotonin, rendering it inactive in the synapses of the brain. It is also known that a dysfunction of the serotonergic system is involved in the development and pathophysiology of affective disorders such as anxiety (Lowry et al., 2008; Owens & Nemeroff, 1994). Moreover, previous studies found that MAO inhibitors were effective in treating emotional disorders (Libert et al., 2011; Reif et al., 2014), and that these disorders are more prevalent in girls (Abbo et al., 2013; Coughlan et al., 2014; Merikangas et al., 2010a,b). Also, in agreement with our results, a recent longitudinal study conducted with a large cohort found that low expression of MAOA was significantly related to greater happiness in women (Chen et al., 2013).

For girls, the effect of the interaction between environmental factors (SLE) and the MAOA-uVNTR polymorphism was found in generalized anxiety. For the other anxiety subtypes, only the SLE was a significant variable but we know that other genetic predispositions may exist (Arias et al., 2012; Baumann et al., 2013). On the other hand, it is important to note that unlike genetic effects, environmental influences are more time-specific, possible because experiences such as SLE are transient (Trzaskowski, Zavos, Haworth, Plomin, & Eley, 2012).

With regard to social phobia, our data showed that this anxiety subtype presents a pattern of results in the opposite direction to that

of the other anxiety subtypes. MAOA-L boys obtained higher social phobia scores than MAOH-H boys. This leads us to think that social phobia may present a different biological basis from other anxiety subtypes. In line with our results, Samochowiec et al. (2004) found that MAOA-uVNTR does not have a role in social phobia in female patients and suggest that another molecular mechanism may underlie their pathogenesis. Another possible interpretation of our finding is that boys with social phobia may have a hypersensitivity trait for social situations and be more concerned about questions on what opinion their peers have of them. This is related to results obtained by Eisenberg et al. (2007), who found that MAOA-L individuals reported higher trait interpersonal hypersensitivity and showed greater dorsal anterior cingulate cortex activity to social exclusion compared with MAOA-H individuals. Also, Baumann et al. (2013) found that male carriers of the MAOA-L allele who reported more aversive experiences in childhood exhibited a trend for enhanced anxious apprehension. In addition, previous studies have revealed a causal relationship between MAOA-L with behavioral, cognitive, neuroanatomical and neuropharmacological impairments in autism spectrum disorders (ASD) (Cohen et al., 2003; Davis et al., 2008; Yirmiya et al., 2002). Some of these studies suggested a potential role of the MAOA alleles in boys (Cohen et al., 2003; Tassone et al., 2011). These findings indicate that MAOA-L variants may be associated with social relationship problems. In fact, the pathogenesis of social phobia may be related to the pathogenesis of other disorders. There is a possibility, therefore, that social phobia is a premorbid manifestation of other

psychopathological problems (such as schizoid spectrum) but more studies are needed to replicate these results.

With regard to conduct disorder symptoms, despite the "worrier-versus warrior-gene" hypothesis our findings did not show statistically significant results. Despite this, it is also known that males are three times more likely than females to have the MAOA-L genotype, which, in interaction with some form of psychosocial adversity, increases the risk of developing conduct problems such as antisocial behaviors (Byrd & Manuck, 2014; Eme, 2013; Kim-Cohen et al., 2006; Weder et al., 2009).

The present study was subject to certain limitations, such as the lack of a large sample and the lack of data on these subjects up to adulthood. We should also bear in mind that other functional polymorphisms may also be responsible for the development of the emotional and behavioral disorders studied. Nevertheless, the study examined the possible influence of environmental and genetic variables and represents a contribution to the growing body of studies on the relationship between the variant of the MAOA-uVNTR polymorphism and the most frequent child and adolescent psychopathological symptoms. Another strength of this study is that the psychopathological information was provided by the children and their parents. In short, as we hypothesized, our results suggest that MAOA-uVNTR polymorphism alleles were associated with self-reported anxiety and that this relationship depends on gender. In this regard, although our results are weak, they do indicate that the MAOA-uVNTR polymorphism may have role in anxiety. On

the other hand, our findings did not find a significant association between this polymorphism and conduct disorder symptoms. However, the failure to find this association does not exclude a role of the MAOA-uVNTR in the etiology of these symptoms. Further replication studies with large samples are needed to confirm these findings.

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**Table 1** Socio-demographic and psychopathological characteristics of the sample

| | Sample of the third phase | | | |
|---|---|---|---|---|
| | **Total (n=228)** | **Boys (n=85)** | **Girls (n=143)** | ***p*** |
| Age (years) | 13.5 (.9) | 13.5 (.9) | 13.6 (.9) | .319 |
| Gender (%) | | 37.3 | 62.7 | |
| **Socioeconomic level** | | | | |
| Low (%) | 34.6 | 32.9 | 34.6 | .699 |
| Medium (%) | 44.7 | 43.5 | 44.7 | |
| High (%) | 20.6 | 23.5 | 20.6 | |
| **Family type** | | | | |
| Nuclear (%) | 83.8 | 87.1 | 81.8 | .299 |
| Single parent (%) | 16.2 | 12.9 | 18.2 | |
| **Birthplace** | | | | |
| Native (%) | 90.4 | 89.4 | 90.9 | .711 |
| Foreign (%) | 9.6 | 10.6 | 9.1 | |
| **Psychopathological variables** | | | | |
| **SCARED** | **Total (n=228)** *Mean (SD)* | **Boys (n=85)** *Mean (SD)* | **Girls (n=143)** *Mean (SD)* | ***p*** |
| Score: total SCARED | 19.9 (9.5) | 17.9 (8.7) | 21.1 (9.8) | .012 |
| Score: somatic/panic | 3.1 (3.1) | 2.2 (2.2) | 3.7 (3.4) | .001 |
| Score: social phobia | 5.3 (3.2) | 5.3 (3.3) | 5.3 (3.2) | .999 |
| Score: generalized anxiety | 6.3 (3.4) | 5.8 (3.4) | 6.6 (3.3) | .085 |
| Score: separation anxiety | 5.2 (3.3) | 4.5 (2.7) | 5.6 (3.6) | .015 |
| **CSI-4** | **Total (n=169)** *Mean (SD)* | **Boys (n=58)** *Mean (SD)* | **Girls (n=111)** *Mean (SD)* | ***p*** |
| Score: attencion deficit symptoms | 7.0 (5.5) | 8.2 (5.6) | 6.5 (5.4) | .057 |
| Score: hyperactivity/impulsivity symptoms | 4.3 (5.0) | 5.2 (7.7) | 3.8 (5.0) | .076 |
| Score: combined ADHD symptoms | 11.3 (9.6) | 13.3 (9.3) | 10.2 (9.7) | .045 |
| Score: oppositional defiant disorder symptoms | 4.9 (4.2) | 4.9 (4.3) | 4.9 (4.2) | .931 |
| Score: conduct disorder symptoms | .7 (1.5) | 1.0 (2.1) | .5 (.9) | .081 |
| Score: generalized anxiety symptoms | 4.3 (3.4) | 4.4 (3.0) | 4.2 (3.5) | .734 |
| Score: specific phobia symptoms | .4 (.7) | .5 (.8) | .4 (.6) | .410 |
| Score: obsessions | .2 (.5) | .3 (.6) | .2 (.5) | .381 |
| Score: compulsions | .1 (.5) | .2 (.6) | .1 (.4) | .555 |
| Score: posttraumatic stress disorder symptoms | .2 (.6) | .2 (.6) | .3 (.6) | .697 |
| Score: separation anxiety symptoms | 1.1 (2.2) | .9 (1.5) | 1.3 (2.4) | .289 |
| Score: social phobia symptoms | 3.1 (1.9) | 3.3 (2.2) | 2.3 (1.7) | .273 |
| Score: major depressive disorder symptoms | 1.6 (2.0) | 1.7 (2.3) | 1.5 (1.8) | .586 |
| Score: dysthymic disorder symptoms | 2.2 (2.3) | 2.3 (2.6) | 2.1 (2.1) | .573 |
| Score: motor tics | .1 (.4) | .3 (.6) | .1 (.3) | .031 |
| Score: vocal tics | .1 (.4) | .2 (.6) | .1 (.3) | .330 |
| Score: schizophrenia | .1 (.4) | .2 (.5) | .1 (.4) | .220 |
| Score: autistic symptoms | 1.8 (2.4) | 2.4 (2.8) | 1.6 (2.1) | .060 |
| Score: asperger symptoms | 1.2 (1.8) | 1.4 (2.0) | 1.1 (1.7) | .237 |

**p* value between boys and girls

**Table 2** Allele and genotype distribution of the MAOA-uVNTR polymorphism of the study sample

| | Alleles, n (%) | | | | | Genotypes, n (%) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **2** | **3** | **3.5** | **4** | **5** | **2/2** | **2/3** | **2/3.5** | **2/4** | **2/5** | **3/3** | **3/4** | **3/3.5** | **3/5** | **3.5/3.5** | **3.5/4** | **3.5/5** | **4/4** | **4/5** | **5/5** |
| **Boys** | 1 (1.2) | 30 (35.3) | 3 (3.5) | 50 (58.8) | 1 (1.2) | 1 (0.1) | - | - | - | - | 30 (4.2) | - | - | - | 3 (.4) | - | - | 50 (7.0) | - | 1 (.1) |
| **Girls** | 1 (.7) | 87 (60.8) | 4 (2.8) | 118 (82.5) | 4 (2.8) | 0 | 1 (.1) | 0 | 0 | 0 | 19 (2.4) | 62 (7.8) | 2 (.3) | 3 (.4) | 0 | 2 (.3) | 0 | 53 (6.7) | 1 (.1) | 0 |
| **Total** | 2 (.9) | 117 (51.3) | 7 (3.1) | 168 (73.7) | 5 (2.2) | 1 (.1) | 1 (.1) | 0 | 0 | 0 | 49 (3.3) | 62 (4.1) | 2 (.1) | 3 (.2) | 3 (.2) | 2 (.1) | 0 | 103 (6.8) | 1 (.1) | 1 (.1) |

**Table 3** Multiple linear regression of the genetic, socio-demographic and environmental variables effect on anxiety, in girls

| | **SCARED Factor 3: Generalized anxiety** | | | |
|---|---|---|---|---|
| | ***B*** | ***t*** | ***p*** | **Model** |
| MAOA | 2.366 | 2.427 | .017 | $R^2$c*100=6.8 |
| Stressful life events | .164 | 2.064 | .042 | $F_{5.101}$=2.484 |
| Age | .181 | .500 | .618 | $p$=.037 |
| SES | .025 | .139 | .890 | |
| Overall academic achievement | .284 | 2.313 | .023 | |

Variables entered into the model: MAOA (0: low-activity; 1: high-activity); Stressful life events (total score); Age (years); SES (total score); Overall academic achievement (total score).

**Table 4** T-test analyses to examine possible differences between the two genotype subgroups (MAOA-L and MAOA-H) for the SCARED and CSI-4 scores, for both genders

| | **Boys** | | | | **Girls** | | | |
|---|---|---|---|---|---|---|---|---|
| | **MAOA - L (SCARED, n=31) (CSI-4, n=23)** | **MAOA-H (SCARED, n=54) (CSI-4, n=35)** | | | **MAOA - L (SCARED, n=20) (CSI-4, n=16)** | **MAOA-H (SCARED, n=123) (CSI-4, n=95)** | | |
| | *Mean (SD)* | *Mean (SD)* | *t* | *p* | *Mean (SD)* | *Mean (SD)* | *t* | *p* |
| SCARED total score (without social phobia factor) | 11.9 (5.0) | 12.9 (7.4) | -.719 | .474 | 13.5 (4.7) | 16.2 (8.8) | -2.033 | **.048** |
| SCARED Factor 1: Somatic/Panic | 2.1 (1.6) | 2.4 (2.5) | -.653 | .515 | 3 (2.4) | 3.8 (3.5) | -1.255 | .218 |
| SCARED Factor 2: Social phobia | 6.4 (3.3) | 4.7 (3.2) | 2.271 | **.026** | 6.3 (2.8) | 5.2 (3.2) | 1.414 | .160 |
| SCARED Factor 3: Generalized anxiety | 5.8 (3.0) | 5.8 (3.6) | .037 | .970 | 5.3 (2.7) | 6.8 (3.4) | -1.873 | .063 |
| SCARED Factor 4: Separation anxiety | 4.0 (2.6) | 4.8 (2.8) | -1.336 | .185 | 5.2 (2.4) | 5.6 (3.8) | -.653 | .518 |
| Any disruptive disorder (CSI-4) | 33.5 (26.9) | 32.3 (20.5) | .191 | .849 | 24.3 (16.3) | 26.2 (23.7) | -.316 | .753 |
| Any emotional disorder (CSI-4) | 14.7 (10.3) | 13.3 (8.5) | .539 | .592 | 11.1 (10.1) | 13.5 (9.3) | -.938 | .350 |

*Values in bold represents $p < .05$.

# 6. Discussió

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 6. Discussió

El present estudi va ser dut a terme a partir d'una mostra representativa d'escolars, procedents d'escoles públiques i privades de la ciutat de Reus, que van ser seguits en tres períodes. La majoria dels nens que van conformar la mostra provenien d'entorns amb un estatus socioeconòmic mig-elevat, eren de nacionalitat espanyola i la seva estructura familiar era majoritàriament de tipus nuclear. L'objectiu principal va ser analitzar la trajectòria dels trastorns emocionals fins a l'inici de l'adolescència. També, avaluar els factors de risc i factors associats a aquests símptomes o trastorns psicopatològics, així com conseqüències de la seva presència per a la vida dels subjectes. La recollida d'una gran quantitat de variables sociodemogràfiques, psicopatològiques, antropomètriques i genètiques, ha contribuït a que es poguessin portar a terme aquests objectius.

Tenint en compte un primer objectiu de conèixer quines característiques psicopatològiques i sociodemogràfiques, poden predir o estar associades amb l'aparició primerenca del diagnòstic de TOC, es van utilitzar les dades de la primera i de la segona fase de l'estudi. Considerant dos nivells de severitat d'aquest trastorn, a grans trets es va comprovar que el TOC subclínic, i per tant menys sever, està més relacionat amb la simptomatologia de caire obsessiu com és la preocupació obsessiva o les supersticions, resultat que va en la mateixa direcció que el que van observar Brynska i Wolanczyk (2005). D'altra banda, el TOC clínic (major severitat) es troba més relacionat amb la simptomatologia d'ansietat, com les manifestacions somàtiques o l'ansietat de separació. A més a més, el TOC clínic també està relacionat amb els símptomes compulsius de comprovació, d'ordre i de neteja, la qual cosa també va en la mateixa direcció que el que mostren els resultats de Brynska i Wolanczyk (2005).

En relació amb el resultat que indica que els símptomes d'ansietat de tipus somàtic prediuen el diagnòstic de TOC clínic, les dades són consistents amb les troballes d'Storch i cols. (2008). Aquests autors van observar que aquest tipus d'ansietat és altament prevalent entre subjectes joves amb TOC i a més a més van trobar que la seva presència produeix un gran impacte pel que fa a la clínica del TOC. Per altra banda, en relació amb el resultat que indica que els símptomes d'ansietat de separació també prediuen el TOC clínic, en primer lloc i com s'ha esmentat a l'apartat d'introducció, cal remarcar que l'ansietat de separació és un subtipus d'ansietat que es manifesta de manera més freqüent a la infància (Kossowsky i cols., 2012). També, tal i com van trobar els autors Ballesteros i Ulloa (2011), el TOC és un trastorn que presenta una alta comorbiditat amb l'ansietat de separació. D'altra banda, cal tenir en compte que a vegades pot arribar a ser complicat distingir entre els símptomes d'ansietat de separació i els símptomes obsessius-compulsius, donat que les preocupacions que manifesten els nens que pateixen ansietat de separació, sovint poden tenir un contingut o unes característiques similars als símptomes de tipus obsessiu. En aquest sentit, els nostres resultats també donen suport a les observacions de Mroczkowski i cols. (2011), els quals van suggerir que l'ansietat de separació és un símptoma d'inici primerenc, apareix amb anterioritat als símptomes obsessius-compulsius i pot influir el curs clínic del TOC quan aquest apareix.

A més a més, tot i que se sap que la depressió està altament relacionada amb la simptomatologia TOC, de manera que alguns autors han trobat que apareix com a conseqüència del desgast que poden produir els símptomes del TOC a la vida diària dels subjectes (Storch i cols., 2012), el fet que les dades trobades no indiquin aquesta relació pot voler dir que la depressió pot aparèixer per la presència de símptomes TOC, però a més llarg terme i no en etapes tan primerenques.

Malgrat la coneguda relació entre els trastorns de la conducta alimentària i el TOC (Kim i cols., 2012), en els nostres resultats no s'hi observa que els alts nivells pel que fa a l'índex de massa corporal, siguin un factor de risc per al TOC, cosa que no s'observa en cap dels seus nivells de severitat. En canvi, el TDAH de tipus hiperactiu/impulsiu s'ha vist que està associat amb el TOC de tipus subclínic, resultat que és comparable amb el que van trobar Sheppard i cols. (2010) i Grisham i cols. (2011), que també observen una relació entre ambdós trastorns. En aquest sentit, és important anar en compte quan un subjecte presenta símptomes d'hiperactivitat i impulsivitat i alhora símptomes obsessius-compulsius, ja que pot

ser que es requereixi un tractament diferent per a cada simptomatologia (Geller, 2006). D'altra banda, la relació observada entre els símptomes de TDAH i el diagnòstic de TOC subclínic, també pot explicar-se per ser dos trastorns que presenten disfuncions a nivell del lòbul frontal (Cubillo i cols., 2012; Shaw i cols., 2014).

Els anàlisis realitzats no han mostrat que variables com el gènere, edat, lloc de naixement o tipus de família, fossin factors de risc o estiguessin significativament relacionats amb el TOC, el que ens permet suggerir la nul·la o baixa influència dels factors socioculturals sobre el TOC, tal i com van observar Himle i cols. (2008). D'altra banda, malgrat els resultats obtinguts a partir de l'anàlisi multivariant no mostren que el rendiment acadèmic sigui un factor predictor o associat amb el TOC, a la nostra mostra es va observar que els subjectes que tenien diagnòstic de TOC clínic presentaven un rendiment acadèmic significativament més baix, indicant la interferència que pot causar aquest trastorn en el funcionament acadèmic dels subjectes (Canals i cols., 2012c). Els resultats també mostren que hi pot haver una relació entre les manifestacions del TOC clínic i el fet de provenir d'un entorn amb un baix nivell socioeconòmic. En aquest sentit els diferents estudis presenten controvèrsies. Així, mentre autors com Degonda i cols. (1993) relacionen la presència dels símptomes obsessius-compulsius amb persones d'entorns socioeconòmics més elevats, d'altres com Heyman i cols. (2001) observen resultats en la mateixa direcció que els nostres. Reiss (2013) va observar que els subjectes procedents de famílies amb clars desavantatges a nivell socioeconòmic, eren dues o tres vegades més propensos a experimentar algun trastorn mental. Per tant, les troballes ens permeten suggerir que les persones que viuen en entorns socioeconòmics més desafavorits, són més vulnerables per desenvolupar algun trastorn mental. Considerant totes aquestes dades, pot ser que la manca de recursos econòmics familiars suposi que els subjectes no acudeixin a un especialista per tal de consultar el seu problema i per tant, aquests subjectes tampoc acabaran rebent el tractament corresponent.

De manera global, a partir dels anàlisis s'observa que l'ansietat prèvia i la simptomatologia TOC prèvia, són les variables més rellevants per sobre de les variables sociodemogràfiques o antropomètriques. El fet de tenir en compte diferents nivells de severitat del TOC és un aspecte força positiu perquè segons han indicat els resultats, l'estudi dels factors predictors i factors relacionats mostra que el TOC subclínic presenta un patró de símptomes obsessius, mentre que el TOC

clínic presenta un patró més relacionat amb els símptomes compulsius i d'ansietat. Per tant, ambdós tipus de diagnòstics presenten patrons diferenciats de símptomes psicopatològics predictors i associats, no recolzant la hipòtesi de continuïtat dels dos nivells de severitat diagnòstica. Però si bé els resultats de l'estudi dels predictors del diangòstic de TOC van en aquesta direcció, l'estudi dels predictors de la simptomatologia obsessiva-compulsiva a llarg terme sí que corrobora l'existència d'una continuïtat d'aquests símptomes dins de l'espectre obsessiu-compulsiu.

En aquest sentit i amb l'objectiu d'estudiar el TOC de manera evolutiva i veure com és el seu curs, es va realitzar el seguiment de la mostra. Així, un altre objectiu va ser l'estudi de la prevalença, persistència, recurrència i incidència dels símptomes obsessius-compulsius, segons dos nivells de severitat. A més a més, també es va voler veure quins factors psicopatològics podien estar influint sobre la presència de manifestacions obsessives-compulsives, a la darrera fase de l'estudi.

La taxa de persistència pel que fa als símptomes obsessius-compulsius (tenint en compte dos nivells de severitat) oscil·la entre un 9,3% i un 28,4%. Són taxes de persistència considerables i que indiquen la cronicitat d'aquests símptomes al llarg del període estudiat. Per altra banda, s'observa que aquesta cronicitat augmenta si es tenen en compte les taxes de recurrència observades i que oscil·len entre un 15,8% i un 21,6%. Per tant, els resultats assenyalen que el TOC es pot considerar un trastorn psicopatològic crònic, les manifestacions del qual es presenten de manera contínua al llarg del temps. Però cal tenir en compte també, que aquestes manifestacions poden presentar fluctuacions pel que fa a la seva severitat, tal i com mostren les taxes de recurrència observades i tal i com van suggerir d'altres autors (Grisham i cols., 2011; Micali i cols., 2010). A més a més, un altre resultat a tenir en compte són les taxes d'incidència de les manifestacions obsessives-compulsives (1,1% - 14,4%), les quals van ser molt més altes que les observades en d'altres estudis (De Graaf i cols., 2002; Veldhuis i cols., 2012). De fet, tant els valors d'incidència, persistència, com recurrència, són difícilment comparables amb els obtinguts en d'altres estudis, degut probablement a les diferències a nivell metodològic. Les taxes d'incidència són un indicador que l'entrada a l'etapa de l'adolescència i la pròpia etapa de l'adolescència, són mereixedores d'atenció en l'estudi del TOC a nivell evolutiu.

Amb l'objectiu concret d'analitzar quins eren els predictors de la simptomatologia TOC (segons els dos nivells de severitat) a l'inici de l'adolescència, es van realitzar

dos models de regressió logística amb tres passos cadascun. En termes generals, els resultats mostren que els símptomes compulsius i d'ansietat de separació previs, són predictors d'ambdós nivells de severitat dels símptomes TOC. Aquestes troballes van en la mateixa direcció que els resultats observats en relació al diagnòstic de TOC clínic i permeten confirmar la continuïtat de les manifestacions obsessives-compulsives al llarg del temps, tenint en compte diferents nivells de severitat. Els resultats també mostren que el factor superstició del LOI-CV és un factor rellevant i a tenir en compte, ja que és un bon predictor de les manifestacions del TOC a la tercera fase. Concretament, el factor superstició i compulsions mentals, és un bon predictor dels símptomes TOC més severs, donat que en aquest cas apareix com un predictor de manera consistent al llarg del temps. Tanmateix les supersticions van estar relacionades amb el diagnòstic de TOC subclínic a la segona fase de l'estudi. D'altra banda, si bé l'ansietat de separació es va trobar relacionada amb el diagnòstic de TOC clínic, en l'estudi prospectiu de símptomes l'ansietat de separació i la fòbia social són també factors predictors dels símptomes menys severs (obsessivitat). Els resultats d'aquest estudi també ens permeten interpretar que hi ha una expressió variable dels símptomes TOC, que en qualsevol cas recolza la coexistència entre els símptomes de l'ansietat i els del TOC. En aquest sentit, Angst i cols. (2004) van trobar que en adults, la prevalença de TOC es veia incrementada de manera significativa en els casos en que els subjectes presentaven fòbia social, mentre que Assunçao i cols. (2012) van trobar uns alts percentatges de comorbiditat entre el TOC i la fòbia social. Pel que fa a la relació amb l'ansietat de separació, la interpretació dels resultats és la mateixa que quan es va trobar aquesta mateixa relació en l'estudi dels factors predictors dels diagnòstics de TOC. L'ansietat de separació es manifesta de manera molt freqüent en les primeres etapes del desenvolupament, i un cop més queda demostrat que pot exercir una gran influència en el curs dels símptomes TOC (Mroczkowski i cols., 2011). A més a més, el fet que les dades assenyalen que l'ansietat de separació és un factor predictor d'ambdós tipus de símptomes obsessius-compulsius, indica que els símptomes d'ansietat pot ser que siguin un factor preexistent, és a dir, que apareguin amb anterioritat a les manifestacions del TOC al llarg del desenvolupament. Dades que van en la mateixa direcció que els resultats de Jakubovski i cols. (2013), els quals observen un pitjor curs del TOC en els casos en que hi havia una història familiar prèvia de presència de símptomes d'ansietat.

Els resultats també van mostrar una relació entre els símptomes depressius i la presència de símptomes obsessius-compulsius més severs a la tercera fase, permetent suggerir que la simptomatologia depressiva més aviat apareix en aquells casos en els que el TOC es presenta de manera més severa i causant per tant una major interferència i desgast en el dia a dia del subjecte que el pateix (Abramowitz i cols., 2007).

Tant els resultats relatius a les taxes de prevalença, persistència, recurrència i incidència com els resultats sobre els factors predictors i relacionats amb la simptomatologia obsessiva-compulsiva, donen suport a la importància de tenir en compte dos punts de tall al LOI-CV, i per tant dos nivells de severitat de les manifestacions del TOC.

Amb objectius molt similars, es va realitzar un article de seguiment sobre el curs dels símptomes d'ansietat. Després d'haver administrat l'SCARED en tres períodes evolutius dels subjectes, i tenint en compte que a banda del punt de tall de l'SCARED, el qual està validat (Canals i cols., 2012a), disposàvem dels punts de tall també validats per a cadascun dels seus factors, en aquest estudi es va poder realitzar un anàlisi força ampli del curs dels símptomes d'ansietat.

De manera general, els resultats mostren que malgrat les puntuacions a l'SCARED disminueixen a través de les diferents etapes, la prevalença de símptomes (tenint en compte el punt de tall 25 a l'SCARED; Birmaher i cols., 1997; Canals i cols., 2012a) és alta i l'ansietat pot continuar manifestant-se al llarg del temps tal i com indiquen les taxes de persistència que s'eleven a més d'un 50%. En aquest sentit, alguns autors que han realitzat importants estudis de seguiment sobre els símptomes d'ansietat, suggereixen que aquests símptomes presenten taxes elevades i estables durant l'inici de l'adolescència (Gullone i cols., 2001; Leikanger i cols., 2012). Pel que fa a les dades d'incidència, s'observa que són majors a la segona fase respecte a la tercera, la qual cosa pot estar relacionada amb el fet que l'ansietat acostuma a presentar-se en etapes primerenques del desenvolupament. D'altra banda, els casos nous a la tercera fase podrien explicar-se pel fet que l'adolescent és més vulnerable per afrontar les situacions socials, familiars i acadèmiques que l'envolten, encara que no podem concloure si aquesta ansietat serà evolutivament transitòria o un inici de problemes cap a l'edat adulta.

Tenint en compte que a les primeres etapes de l'adolescència la fòbia social és un subtipus d'ansietat altament prevalent (Beesdo i cols., 2012; Gren-Landell i cols., 2009), els nostres resultats corroboren aquesta informació, ja que s'observa que la fòbia social és el subtipus d'ansietat que presenta una major taxa de prevalença (55,6%), persistència a major (46,8%) i a menor (68,9%) termini, i d'incidència (25,9% - 40,7%). A més a més, la fòbia social s'ha vist que també és un predictor rellevant de la persistència de l'ansietat i dels símptomes TOC. Això indica que és molt important la seva detecció primerenca, a fi d'evitar que l'ansietat presenti un curs crònic o cursi amb un pitjor pronòstic, com suposaria l'aparició d'un problema associat relacionat amb el trastorn d'abús de substàncies (Buckner i cols., 2008), trastorns de l'humor (Duffy i cols., 2013) o trastorns de tipus psicòtic (Granö i cols., 2012; Wigman i cols., 2012).

L'ansietat generalitzada és l'altre subtipus d'ansietat que també presenta altes taxes de prevalença (44,4%), persistència (41% - 63%) i incidència (26,2% - 34,8%). A més a més no s'observa una disminució significativa de les puntuacions en aquest factor de la segona a la tercera fase, la qual cosa és consistent amb les troballes de Van Oort i cols. (2009), els quals suggereixen que l'ansietat generalitzada presenta un increment a l'adolescència. Tant la fòbia social, com l'ansietat generalitzada i també els símptomes d'ansietat de separació, són importants predictors de la persistència de l'ansietat al llarg del temps. Per tant, els resultats posen de rellevància la importància de la detecció primerenca de l'ansietat.

Considerant la variable gènere, tal i com s'ha observat en d'altres estudis, en general les nenes presenten majors taxes de prevalença i persistència de símptomes d'ansietat en comparació amb els nens (Orgilés i cols., 2012; Van Oort i cols., 2009). Concretament, les nenes presenten significativament més símptomes prevalents i persistents d'ansietat social i d'ansietat generalitzada. Així, també es pot observar que a la tercera fase, les puntuacions a l'SCARED obtingudes per les nenes són superiors a les obtingudes pels nens, és a dir a l'inici de l'adolescència les nenes presenten puntuacions més elevades en ansietat. Aquest resultat és un indicador que l'ansietat, en el cas del sexe femení, augmenta a mesura que els subjectes es fan grans. L'ansietat de tipus somàtic és un dels subtipus que a la tercera fase es presenta en major quantitat i de forma estadísticament significativa, en el cas de les nenes. En canvi, a la primera fase són els nens els qui obtenen puntuacions significativament superiors per al factor d'ansietat somàtica, la qual

cosa no és consistent amb els resultats previs (Essau i cols., 2013). De la mateixa manera, cal destacar que els resultats també mostren que el sexe masculí actua com un factor protector dels símptomes crònics d'ansietat. Aquestes diferències entre ambdós sexes poden ser degudes a una predisposició de tipus genètic (Franic i cols., 2010).

També es va voler observar, si els subjectes que havien presentat ansietat persistent al llarg de les tres fases, presentaven uns majors índexs de co-ocurrència d'altres símptomes psicopatològics, en comparació amb els subjectes que no havien obtingut punts de tall elevats a l'SCARED en cap de les tres fases. Els resultats van anar en la direcció que s'esperava, per tant els subjectes que van presentar ansietat de manera persistent al llarg del temps, presentaven alhora altes puntuacions en depressió, símptomes obsessius, bulímia i tics de tipus vocals. Pel que fa a la relació entre l'ansietat i els símptomes depressius, aquests resultats són congruents amb els obtinguts per altres autors que també van realitzar els seus estudis amb subjectes que es trobaven en etapes primerenques del desenvolupament (Masi i cols., 2004; Mathew i cols., 2011). A més a més, s'ha pogut observar que les puntuacions obtingudes al qüestionari de símptomes depressius (CDI) són un predictor rellevant de la persistència de l'ansietat. Per tant, tot sembla indicar que l'ansietat de tipus més sever, l'ansietat que es presenta de forma persistent, està altament relacionada amb la depressió. Probablement, i a part de la vulnerabilitat genètica entre ambdós patologies, el subjecte amb severitat dels símptomes d'ansietat pot tenir complicacions a l'hora d'afrontar els diversos aspectes de la seva vida diària i per tant patir un fort desgast a nivell emocional, la qual cosa pot acabar desencadenant l'aparició de símptomes relacionats amb el trastorn depressiu. En aquest sentit, també s'ha observat que els subjectes que presenten ansietat de separació de forma persistent al llarg de les primeres etapes de la vida, presenten també alts índex de co-ocurrència d'altres símptomes psicopatològics, en la mateixa direcció que el que s'afirma a l'estudi de Kossowsky i cols. (2012) sobre que l'ansietat de separació té un pronòstic desfavorable al llarg del temps. Per tant, sintetitzant els resultats entorn a l'ansietat de separació, es pot observar que per una banda i tenint en compte els anàlisis de regressió logística, la presència primerenca de símptomes d'ansietat de separació està altament relacionada amb la persistència de l'ansietat. I per altra banda, quan aquest

subtipus d'ansietat persisteix en el temps, això és un indicador que aquests subjectes tenen un alt risc de presentar d'altres símptomes associats.

Pel que fa a l'associació entre l'ansietat persistent i les variables rendiment acadèmic i qualitat de la relació amb els iguals, només es van trobar resultats significatius per a la primera. Els resultats indiquen que els subjectes que presenten un millor rendiment acadèmic, són aquells que no presenten ansietat de manera persistent. Per tant, d'acord amb la hipòtesi plantejada, els resultats mostren que l'ansietat crònica i severa pot implicar interferències notables en un dels punts clau de la vida dels subjectes a aquestes edats, és a dir, l'àmbit escolar. Tanmateix cal recordar que en aquest estudi s'utilitzen dades sobre simptomatologia d'ansietat i no es treballa amb diagnòstics. En aquest sentit, això podria explicar que no s'hagués trobat una relació entre la persistència de la simptomatologia d'ansietat i la presència de problemes a nivell social de relació amb els iguals, entre d'altres possibles explicacions com seria el fet que els pares podrien ser uns mals informants sobre com són les relacions socials dels seus fills.

Conèixer millor el curs de l'ansietat en aquestes etapes, i poder identificar aquells factors que precedeixen les manifestacions d'ansietat, les mantenen o en fan empitjorar el curs, són aspectes fonamentals a fi de poder aplicar una millor intervenció i millorar-ne el pronòstic.

Després d'una exhaustiva revisió bibliogràfica d'estudis epidemiològics en psicopatologia infantil i juvenil, una de les conclusions que s'hi poden observar de forma generalitzada és la manca d'estudis de seguiment de psicopatologia en general, però també una manca d'estudis amb l'objectiu de fer un seguiment concret dels diferents trastorns psicopatològics i simptomatologia que afecta en major mesura als nens i nenes i adolescents actualment. Se sap que el curs d'un determinat trastorn psicopatològic està altament relacionat amb els estadis del desenvolupament pels que va passant un individu. Per aquest motiu, els estudis de seguiment en població no clínica permeten ampliar el coneixement sobre com evolucionen els diferents trastorns mentals, sabent que molts trastorns de l'edat adulta comencen o tenen les seves arrels en la infància o l'adolescència. És per això que l'epidemiologia psiquiàtrica requereix un enfoc evolutiu (Cannon i cols., 2002; Elder, 1998). Tant l'article sobre factors predictors i associats amb els diagnòstics de TOC, com els articles de seguiment sobre la simptomatologia obsessiva-compulsiva

o la simptomatologia d'ansietat, suposen una contribució a aquesta manca d'estudis.

Quant a l'estudi de la influència dels trastorns emocionals sobre el rendiment acadèmic dels adolescents, en aquest senit per una banda sabem que el present estudi està realitzat amb subjectes que es troben en època d'estar escolaritzats i a més a més, la tercera fase coincideix amb l'inici del període de l'adolescència, època de grans canvis i que s'ha relacionat amb problemes a nivell acadèmic i amb la presència d'una major quantitat de símptomes psicopatològics. Per l'altra, sabem que el fracàs escolar és una de les majors preocupacions que presenta el sistema educatiu espanyol, ja que les taxes són de les més elevades en relació a la resta de països de la Unió Europea (Calero i cols., 2010). És per aquests motius que es va hipotetitzar que el rendiment acadèmic dels adolescents sí que es podria veure afectat per la presència de símptomes emocionals. En primer lloc, els resultats van mostrar que la simptomatologia emocional prèvia exerceix una clara influència sobre els resultats acadèmics obtinguts a l'adolescència. Pel que fa als símptomes depressius previs, aquesta variable va ser la que es va observar, de manera més consistent, com un factor predictor del rendiment acadèmic en qualsevol àrea de coneixement, troballa que és recolzada per d'altres estudis (Fröjd i cols., 2008). En aquest sentit els símptomes depressius com l'apatia, l'anhedonia, la irritabilitat o la sensació de tristesa, poden produir una reducció dels recursos cognitius disponibles, dèficits pel que fa a la memòria de treball o als mecanismes relacionats amb la motivació, que acaben causant serioses dificultats i interferències significatives a nivell acadèmic. Seguint amb la influència de la simptomatologia emocional, els resultats també indiquen que quan l'ansietat es presenta de manera persistent, i com ja s'ha comentat anteriorment, això causa interferències a nivell escolar. Pel que fa a l'ansietat de separació, els resultats han mostrat que la presència d'aquest subtipus d'ansietat afecta negativament al rendiment acadèmic. Quan els subjectes arriben a l'adolescència, degut a ser una època de transició, és possible que avaluïn com és el vincle amb els seus progenitors i cuidadors, de tal manera que necessiten sentir-se segurs i quan això no és així, es poden tornar més vulnerables i acabar desenvolupant algun trastorn d'ansietat com seria l'ansietat de separació (Esbjorn i cols., 2012).

Tanmateix, els resultats mostren que l'ansietat no sempre influeix negativament al rendiment acadèmic. L'ansietat generalitzada i la fòbia social presenten una relació positiva amb el rendiment acadèmic, de manera que la presència de nivells moderats d'aquests símptomes s'associa a un rendiment acadèmic més elevat. Així, els subjectes que presenten nivells moderats d'ansietat generalitzada probablement són subjectes preocupats pels seus estudis, és un tipus d'ansietat que els manté en alerta i en tensió i comporta que rendeixin millor. Pel que fa a l'ansietat social, com ja s'ha dit, els resultats van en la mateixa direcció. Probablement, i d'acord amb Eysenck i Derakshan (2011), són subjectes que estan altament motivats per realitzar les tasques escolars de manera correcta, amb la finalitat d'evitar qualsevol opinió o crítica negativa per part dels iguals o dels seus mestres o pares. En aquest sentit, també és important destacar els resultats observats per Owens i cols. (2014) que van una mica més enllà del que exposen Eysenck i Derakshan (2011). Owens i cols. (2014) van observar que els subjectes que presenten símptomes d'ansietat, si alhora són subjectes amb una alta capacitat de memòria de treball, aquests tindran suficients recursos per manejar correctament aquesta motivació per a realitzar les tasques escolars de manera adequada, i així els resultats acadèmics seran millors. Però per altra banda, també cal tenir en compte que l'ansietat pot ser precisament un factor que interfereixi en la memòria de treball, causant pitjors resultats acadèmics (Aronen i cols., 2005).

Un dels trastorns psicopatològics que s'ha vist que afecta en gran mesura al rendiment acadèmic és el TDAH. Així, el TDAH comporta problemes a nivell de les funcions executives, incapacitat per a mantenir l'atenció i també pot implicar problemes de conducta, els quals poden produir un impacte negatiu en els resultats acadèmics dels escolars, i en especial durant l'adolescència (Langberg i cols., 2013; Scholtens i cols., 2013; Sijtema i cols., 2013). Els resultats mostren que el TDAH està relacionat de manera consistent amb el baix rendiment acadèmic. En aquest sentit es pot observar que, a la segona fase de l'estudi, el diagnòstic de TDAH de tipus combinat apareix com a variable estadísticament significativa per sobre dels altres tipus de diagnòstics de TDAH. També, a la tercera fase es pot observar com la simptomatologia TDAH, i per tant sense ser tan interferent com ho és el fet de tenir el diagnòstic, també apareix com una variable que influeix de manera negativa a nivell acadèmic.

Quant als factors de tipus sociodemogràfic en relació amb el rendiment acadèmic, no s'observen resultats concloents en relació a variables com el lloc de naixement, el gènere, l'edat o el tipus de família. L'única variable sociodemogràfica que s'ha trobat que influeix al rendiment acadèmic és el nivell socioeconòmic. En aquest sentit, els resultats mostren de manera consistent i en especial en el cas del rendiment en matemàtiques, que els subjectes que provenen d'ambients amb un alt nivell socioeconòmic, obtenen millors resultats acadèmics, troballa que va en la mateixa direcció que els resultats d'estudis anteriors (Caro i cols., 2009; Srin, 2005). Això pot ser degut a que els pares d'aquests nens és probable que hagin assolit nivells acadèmics més alts pel fet de tenir més recursos, d'aquesta manera també estaran més preparats per ajudar als seus fills en les tasques acadèmiques. També és possible que tinguin feines de major prestigi, que siguin més exigents amb els seus fills, que valorin més l'educació, o que se sentin més còmodes en l'entorn educatiu, entre d'altres qüestions.

Els nostres resultats contribueixen al coneixement de factors de risc que poden predisposar al fracàs escolar en els nostres adolescents. A part dels trastorns d'aprenentatge i el TDAH, identificar problemes emocionals relacionats amb la depressió i l'ansietat i portar a terme intervencions eficaces, serà crucial a fi de prevenir que es produeixin altes taxes de fracàs escolar o d'altres conseqüències com l'abandonament escolar prematur.

L'estudi de l'etiologia dels trastorns emocionals i de conducta, també inclou els estudis de genètica, ja que com s'ha esmentat, els factors de risc de tipus genètic són molt importants i de cada cop proliferen més les investigacions en aquest sentit. Degut a la coneguda influència dels al·lels del polimorfisme del gen MAOA (MAOA-uVNTR) sobre la fisiologia i comportament humà, un altre objectiu va ser analitzar la possible associació entre aquest polimorfisme i diversos símptomes psicopatològics altament prevalents en els adolescents. Els resultats mostren que la relació que els al·lels del polimorfisme del gen MAOA tenen amb la presència de determinats símptomes psicopatològics, depèn del gènere dels subjectes. Així, s'ha observat que els subjectes del sexe femení que tenen una alta activitat del polimorfisme del gen MAOA, presenten majors puntuacions a l'SCARED total i també pel que fa a l'ansietat generalitzada. En aquest sentit són varis els estudis, però majoritàriament realitzats amb mostres d'adults, que observen resultats en la mateixa direcció (Chen

i cols., 2013b; Rivera i cols., 2009; Yu i cols., 2005). De fet, a nivell biològic una alta activitat del polimorfisme MAOA-uVNTR implica que es produeixi una major degradació de serotonina. Alhora, una disfunció a nivell del sistema serotoninèrgic s'ha vist que està clarament relacionada amb la presència de trastorns afectius (Lowry i cols., 2008). També, a nivell farmacològic s'ha observat que l'ús dels inhibidors de la MAO, que impliquen l'augment dels nivells de serotonina al cervell, poden ser efectius en el tractament de l'ansietat en persones que tenen una alta activitat del polimorfisme MAOA-uVNTR (Zalsman i cols., 2011). Sobre la relació entre el polimorfisme estudiat i la presència d'ansietat generalitzada, cal dir que els resultats també han mostrat la influència dels esdeveniments vitals estressants viscuts, tal i com s'observa en estudis previs sobre la interacció entre la genètica i l'ambient (Baumann i cols., 2013; Waszczuk i cols., 2013).

Els resultats també mostren que en el cas de la fòbia social, són els subjectes del sexe masculí i amb una baixa activitat del polimorfisme MAOA-uVNTR, els que presenten significativament una major quantitat de símptomes d'aquest subtipus d'ansietat. Aquests resultats mostren que l'ansietat social no sembla presentar un patró que vagi en la mateixa direcció que la resta de trastorns d'ansietat (en els que s'observa una tendència a que presentin majors nivells de somatitzacions i trastorn de pànic, d'ansietat generalitzada i d'ansietat de separació, els subjectes amb una alta activitat del polimorfisme). La interpretació d'aquest resultat pot anar en la mateixa direcció que els estudis previs, si es té en compte que els subjectes amb una baixa activitat del polimorfisme MAOA-uVNTR són subjectes que poden presentar una hipersensibilitat i una major reactivitat davant determinades situacions socials (Baumann i cols., 2013; Eisenberg i cols., 2007). Per altra banda, una altra interpretació podria ser que la patogènesi de l'ansietat de tipus social fos diferent en relació a la patogènesi dels altres subtipus d'ansietat (Samochowiec i cols., 2004). Els resultats previs que relacionen la baixa activitat del polimorfisme MAOA-uVNTR, en el cas dels nens, amb els trastorns de l'espectre autista, ens permeten hipotetitzar que potser en alguns casos l'ansietat social es podria considerar una manifestació premòrbida d'altres manifestacions psicopatològiques (com per exemple manifestacions dins de l'espectre esquizoide) (Cohen i cols., 2003; Tassone i cols., 2011). Altrament, els resultats no indiquen que a la nostra mostra hi hagi una relació entre els al·lels del polimorfisme del gen MAOA i la presència de símptomes relacionats amb trastorns conductuals. El fet que els resultats no siguin significatius

no vol dir que el polimorfisme MAOA-uVNTR no influeixi en l'etiologia d'aquest tipus de símptomes, és per això que caldria replicar aquests resultats i seguir investigant si realment existeix aquesta relació o no. Una altra qüestió a tenir en compte és que existeixen d'altres polimorfismes que també poden ser responsables d'aquest tipus de símptomes. Així, cal realitzar més estudis, replicar-los en mostres més àmplies i en subjectes de totes les edats i procedents de diferents cultures, també analitzant la influència de varis gens, a fi d'arribar a obtenir resultats més concloents.

Els estudis presentats en aquest treball, i seguint la definició proposada per Caplan (1964), realitzen una aportació al coneixement professional, teòric i pràctic que permetrà aplicar intervencions amb caràcter preventiu, i així poder contribuir a una reducció de la incidència de trastorns mentals, de la duració i de la incapacitat que poden produir per a la vida diària dels qui els pateixen. La prevenció, és el tipus d'intervenció més desitjable per a fer front als trastorns psicopatològics (Ezpeleta, 2005). Conèixer els factors de risc que contribueixen a l'aparició de determinades manifestacions psicopatològiques, o que contribueixen al seu empitjorament i pitjor pronòstic, és un coneixement útil per tal d'intervenir de manera preventiva. En aquest sentit, les intervencions preventives permeten contrarestar els efectes dels factors de risc i potenciar l'efecte dels factors de protecció (Ezpeleta, 2005).

Una altra de les contribucions realitzades a través d'aquests estudis, està relacionada amb l'augment de coneixement sobre dades epidemiològiques de l'ansietat i del TOC en el nostre entorn. En epidemiologia és molt important la realització d'estudis de seguiment, no només l'estudi de la prevalença. Així, és important el concepte d'epidemiologia del desenvolupament (Kellam i cols., 1977) que es relaciona amb la importància de comprendre els principis del desenvolupament humà (a nivell biològic, social i cultural) per tal d'entendre l'epidemiologia dels trastorns psiquiàtrics, donat que el curs d'un determinat trastorn psicopatològic està íntimament lligat amb l'estadi del desenvolupament al qual es troba l'individu amb risc.

Amb tot, la realització d'una major quantitat d'estudis de seguiment, tractant de pal·liar problemes com l'ús de metodologies tan diferenciades, o unificant criteris per a la detecció de problemes psicopatològics, és el que comportaria que es realitzés un veritable avenç en epidemiologia. D'aquesta manera es disposaria del coneixement necessari i més sòlid, que permetria que es poguessin realitzar cada

vegada més intervencions preventives de tipus primari i secundari. Així, es podria ajudar a reduir l'alta prevalença de trastorns mentals en nens i adolescents que existeix i que poden continuar a l'edat adulta, i la problemàtica de comunitats que no compten amb els recursos i dispositius necessaris i suficients per atendre a aquesta elevada xifra de casos.

## 6.1. Limitacions

Els estudis presentats en aquesta tesi doctoral tenen certes limitacions que no han de ser passades per alt.

En primer lloc i de manera global, la mida de la mostra no és suficientment gran per a poder fer seguiment dels casos diagnosticats. Així, malgrat que es parteix d'una mostra àmplia (n=1.514), els trastorns diagnosticats constitueixen nombres petits de subjectes. En aquest sentit, tenim una baixa quantitat de subjectes que van presentar un diagnòstic de TOC i per això vam optar per baixar l'exigència de criteris i vam considerar el TOC subclínic. No obstant, aquesta diferenciació pel que fa al nivell de severitat, ha passat a ser un punt fort en l'estudi de l'expressivitat clínica i evolutiva del TOC.

També de manera global, una segona limitació important és la reducció de la mostra de seguiment, limitació que ha afectat especialment als estudis sobre el curs dels símptomes TOC i dels símptomes d'ansietat. A la tercera fase, en la que es va realitzar el seguiment, es va produir una reducció important de la quantitat de consentiments informats obtinguts. Els investigadors van realitzar un veritable esforç per contactar de nou amb tots els subjectes que havien participat a la segona fase. Molts subjectes havien passat de l'escola a l'institut i la tasca de buscar a quin institut de la ciutat s'havien traslladat i contactar-hi de nou, va ser força complexa. A partir d'aquí es va elaborar una carta informativa (amb català i amb castellà), on s'explicava exhaustivament a les famílies en què consistiria la tercera fase i també s'hi adjuntava el consentiment informat. Malgrat la feina feta i els esforços, la resposta de moltes famílies va ser negativa. Tanmateix, en aquells casos en els quals la carta no era retornada amb cap tipus de resposta, es trucava personalment a les famílies de manera que es va aconseguir que el nombre de participants

augmentés una mica. Per tal d'avaluar com podia haver afectat aquest alt percentatge d'abandonament, que per altra banda és un conegut desavantatge dels estudis longitudinals, es van realitzar una sèrie d'anàlisis amb l'objectiu d'examinar possibles diferències entre els subjectes que van participar a la tercera fase i els que van deixar de participar.

# 7.Conclusions

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 7. Conclusions

En relació amb l'objectiu i la hipòtesi generals d'aquesta tesi, s'ha observat a través de les dades de prevalença, persistència i recurrència que tant la simptomatologia obsessiva-compulsiva com la simptomatologia d'ansietat es manifesten de manera crònica al llarg del període estudiat, recolzant així la hipòtesi plantejada. A més a més, també s'ha observat que aquestes manifestacions causen una alta interferència en aspectes psicosocials i acadèmics de la vida de l'adolescent.

**1.-** El TOC clínic i el TOC subclínic tenen dos patrons diferenciats de símptomes psicopatològics predictors i associats. No obstant, si bé això no recolza la hipòtesi de continuïtat dels dos nivells de severitat diagnòstica, l'estudi dels predictors de símptomes TOC a llarg terme corrobora l'existència de l'espectre obsessiu-compulsiu.

**2.-** Els símptomes somàtics i d'ansietat de separació són bons predictors de TOC clínic, mentre que les preocupacions obsessives ho són del TOC subclínic. L'estudi de variables associades recolza en el TOC subclínic un patró de símptomes obsessius, mentre que en el TOC clínic es presenten símptomes compulsius i d'ansietat.

**3.-** El baix nivell socioeconòmic s'associa a la presència de TOC clínic i la simptomatologia TDAH al TOC subclínic.

**4.-** Segons el nivell de severitat dels símptomes obsessius-compulsius, la prevalença oscil·la entre el 4,8% i el 30,4%. La persistència bianual i tri-anual es dóna entre el 9,3% i el 28,4%. Aquesta cronicitat supera el 30% si considerem que

entre el 15,8% i el 21,6% són recurrents en el període dels tres anys. El percentatge de nous casos presentats (incidència entre l'1,1% i el 14,4%) també recolza que l'etapa de l'adolescència és mereixedora d'atenció pel que fa a la patologia obsessiva-compulsiva.

**5.-** Els símptomes compulsius i d'ansietat de separació previs són predictors d'ambdós nivells de severitat dels símptomes TOC. Aquestes dades són coincidents amb les trobades pel que fa al diagnòstic de TOC clínic i ens permeten corroborar la continuïtat de les manifestacions en diferents nivells de severitat.

**6.-** Els símptomes depressius es troben només associats a la simptomatologia TOC més severa a la tercera fase de l'estudi.

**7.-** La persistència de símptomes d'ansietat als tres anys de seguiment va del 32,3% al 55,2%.

**8.-** Els símptomes d'ansietat social són els més prevalents (55,6%), persistents (46,8% - 68,9%) i incidents (26% - 40,7%) a la població estudiada, seguit dels símptomes d'ansietat generalitzada (prevalença: 44,4%; persistència: 41% - 63%; incidència: 26,2% - 34,8%).

**9.-** Les nenes presenten significativament més símptomes prevalents i persistents d'ansietat social i d'ansietat generalitzada que els nens. El sexe masculí és un factor protector dels símptomes crònics d'ansietat en l'adolescent.

**10.-** Els adolescents amb simptomatologia crònica d'ansietat presenten significativament més símptomes obsessius, de tics vocals, depressius i de bulímia, que els que no presenten ansietat crònica.

**11.-** Els símptomes depressius primerencs són la variable consistentment predictora del rendiment acadèmic. Tanmateix, els símptomes d'ansietat persistents i el TDAH, influeixen negativament sobre el rendiment acadèmic dels adolescents. En canvi, determinats nivells d'ansietat generalitzada i d'ansietat social estan relacionats amb un millor rendiment acadèmic.

**12.-** L'alt nivell socioeconòmic de les famílies està positivament relacionat amb el rendiment acadèmic dels adolescents, especialment en el cas del rendiment en matemàtiques.

**13.-** Els al·lels del polimorfisme del gen MAOA (MAOA-uVNTR) presenten una associació amb els símptomes d'ansietat depenent del gènere dels subjectes. Les noies que tenen una alta activitat del polimorfisme del gen MAOA, presenten una major quantitat de símptomes d'ansietat total i d'ansietat generalitzada. Mentre que en el cas dels nois, els subjectes que tenen una baixa activitat del polimorfisme del gen MAOA, presenten majors nivells d'ansietat social.

**14.-** La influència del polimorfisme MAOA-uVNTR sobre l'ansietat generalitzada en el cas de les noies, està relacionada amb la influència també de factors ambientals.

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

# 8. Bibliografia

UNIVERSITAT ROVIRA I VIRGILI
ESTUDI EPIDEMIOLÒGIC PROSPECTIU DE LA SIMPTOMATOLOGIA EMOCIONAL A L'INICI DE L'ADOLESCÈNCIA: SEGUIMENT EN TRES PERÍODES EVOLUTIUS
Núria Voltas Moreso
Dipòsit Legal: T 956-2014

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