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VULNERABILITY FACTORS FOR INTERNALIZING PROBLEMS:

CARDIAC AND AFFECTIVE COMPLEXITY IN ADOLESCENTS UNDER ECOLOGICAL AND LABORATORY CONDITIONS

ANA MARIA FIOL VENY

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Doctoral Programme of *Neuroscience*

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5. Fiol-Veny, A., Balle, M., Fiskum, C., & Bornas, X. (2019). Sex differences in adolescents' cardiac reactivity and recovery under acute stress: the importance of nonlinear measures. *Psychophysiology.* [JCR IF = 3.378]

PREFACE

Adolescence is a transitional period of development in which many biopsychosocial changes take place. Despite all the challenges that adolescents have to face during this stage, most of them will become healthy adults in the future. However, we must not forget this proportion of youths that will probably develop psychopathological problems that will hamper their adjustment in the future. In fact, adolescence is considered a risk period since it marks the median age of onset of many internalizing disorders (IDs), as anxiety and depression. Adolescents who suffer from anxiety and/or depression can go unnoticed for long periods of time inasmuch as they usually keep their problems to themselves or internalize them. As a consequence, it is highly likely that these problems remain stable or increase over the years. Because of all this, adolescence is one of most critical periods to trigger prevention efforts against internalizing problems. In order to develop targeted and efficacious prevention strategies, it is essential to be able to identify those adolescents with higher vulnerability of developing an internalizing disorder in the future.

Traditionally, the scientific study of psychopathology has focused on linear conceptions of human behavior. However, our behavior is nonlinear and highly complex, thus an explanation based on linear terms would be excessively simple. The Dynamic System Theory attempts to solve this reductionism by studying human behavior as it is: a complex nonlinear phenomenon. Even though this approach is relatively new for specialists in Psychology, more and more researchers are venturing into the study of complex human behavior by taking this perspective as a theoretical reference, and several studies have already proved its appropriateness for the study of psychopathology.

Bearing in mind this background, the current thesis aims at responding to some questions still unresolved in the field of adolescent psychopathology, specifically regarding psychological and physiological vulnerability for internalizing disorders, by using the Dynamic Systems Theory as the main theoretical framework. Two general questions were formulated: a) Can cardiac and affective complexity indexes help to distinguish between healthy adolescents more vulnerable and less vulnerable to experience IDs?, b) How are affective and cardiac complexity from healthy adolescents related to other established IDs-related vulnerability factors, such as sex, internalizing symptomatology or emotion dysregulation? Since most of the available evidence on this topic relies on studies conducted in resting conditions, in order to increase the generalization of some conclusions already established by previous literature, the current thesis was intended to provide answers to these questions by studying adolescents when engaged in their daily life and under laboratory induced stress conditions. From this point, a series of specific questions were addressed by five studies:

The study 1 was focused on affective complexity. A previous study by Bornas, Balle, De la Torre-Luque, Fiol-Veny, and Llabrés (2015) proved the multistability of affective fluctuations in a sample of healthy adults. Following these results, the study 1 of the current thesis was intended to discover if healthy adolescents show multistability

in their affective fluctuations, as adults do, and how these affective regulation processes are related to temperamental factors and anxiety symptomatology. This study was developed under ecological conditions. Studies from 2 to 5, were centered on cardiac complexity. The study 2 was focused on determining whether there exist differences in cardiac complexity between healthy adolescents with high and low levels of anxiety symptoms, and between females and males, under ecological conditions. The interaction between these two factors was also explored. Another key question of the current thesis was whether there exist sex differences in cardiac complexity of healthy adolescents, regardless their level of anxiety symptomatology. Sex differences were already explored in the study 2, but they were linked to the adolescents' anxiety symptomatology level (only groups with high and low anxiety were used). Furthermore, the sample size turned out to be very small. In order to solve this problem, for the study 3, a higher simple size of adolescents was randomly selected in order to obtain a sample that covered all ranges of anxiety symptoms. This study was also performed under ecological conditions and addressed at how cardiac complexity and internalizing symptoms are related. Regarding the study 4, the main objective was to discover how cardiac complexity properties of healthy adolescents are related to cognitive emotional regulation strategies in front of elicited stress under laboratory settings. Finally, the study 5 was designed for investigating sex differences in cardiac complexity of healthy adolescents, under laboratory stressful conditions.

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Aina Fiol Veny

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CONTENTS

Abstract

The internalizing disorders (IDs) are the highest prevalent psychopathological conditions in adults and cause great impairment in several areas of the individual and their relatives. Since adolescence marks the median age of onset for many IDs, it is considered a risk period for their development. Unfortunately, these problems are not sufficiently detected in primary care and the probability of maintaining an ID from adolescence to adulthood is high. The study of related vulnerability factors can help to disentangle the genesis and the maintenance of IDs, and consequently to design empirically based prevention and intervention programs. As far as we know, the evidence in adolescent population is still scarce.

Traditionally, the study of psychopathology has focused on linear conceptions of human behavior. The Dynamic System Theory (DST), a recent perspective in the field of Psychology, can be a useful strategy for understanding human behavior as it is, a complex nonlinear phenomenon.

The main objective of the present thesis was to overcome some gaps regarding the psychological and physiological vulnerability for IDs in adolescents, using the DST as the main theoretical framework. Two general questions were tried to answer: a) Can cardiac and affective complexity indexes help to distinguish between healthy adolescents more vulnerable and less vulnerable to experience IDs?, b) How are affective and cardiac complexity from healthy adolescents related to other established IDs-related vulnerability factors, such as sex, internalizing symptomatology or emotion dysregulation?

Five studies were designed in ecological or laboratory conditions, in order to obtain a better representation of cardiovascular and affective dynamics. In the study 1, a sample of healthy adolescents reported their daily mood, anxiety and worry levels twice a day over a period of 100 days. In the studies 2 and 3, the cardiac activity of healthy adolescents was recorded during 120 minutes while performing regular activities within the academic context. The sample of the study 2 was divided into two groups according to sex (male/female) and anxiety symptoms level (high/low). The sample of the study 3 was randomly selected, regardless of their level of anxiety symptoms. In the studies 4 and 5, the cardiac activity of healthy adolescents was recorded while performing a socially relevant stress induction protocol. The emotion regulation style of the participants from the study 4 was also assessed.

Almost all scaling exponents proved their fractal nature and multistability. Furthermore, worry exponents were positively correlated with effortful control, and negatively associated with negative affectivity and affiliativeness (study 1). Regarding cardiac complexity, it was found to be lower in females in comparison to males (study 2, 3 and 5), as well as in adolescents prone to engage in more negative emotion regulation strategies in general, but only when they switched from stress to recovery (study 4). Prediction analyses showed that the lower the cardiac complexity, the higher the

internalizing symptoms (study 3). Finally, the female sex predicted a lower cardiac complexity, but the negative emotion regulation style was positively related to cardiac complexity (study 4).

In summary, this doctoral thesis proves that the affective and cardiac fluctuations of healthy adolescents are under complex regulation processes that have memory and take into account information from different time scales, to successfully adapt to their daily life. It is also concluded that healthy adolescents more vulnerable to IDs (females, higher internalizing symptoms or emotion dysregulation strategies) seem to have lower levels of affective and cardiac complexity than less vulnerable adolescents. Therefore, this attenuated cardiac and affective flexibility/complexity may constitute physiological and psychological markers of a maladaptive pattern to confront internal and environmental challenges.

Resum

Els trastorns internalitzants (TIs) són les psicopatologies amb major prevalença en adults i generen un gran deteriorament en moltes àrees de la persona i dels seus familiars. L'edat mitjana d'inici de molts d'aquests trastorns s'emmarca dins l'adolescència, motiu pel qual aquesta etapa és considerada un període de risc per al desenvolupament de TIs. La probabilitat que un TI es mantingui de l'adolescència fins a l'edat adulta és elevada, ja que aquests problemes no són suficientment detectats pels sistemes d'atenció primerenca. En aquest sentit, l'estudi de factors de vulnerabilitat relacionats amb els TIs pot ajudar a esclarir la gènesi i el manteniment d'aquests trastorns i, conseqüentment, ajudar a dissenyar programes de prevenció i d'intervenció basats en l'evidència empírica. Pel que sabem, l'evidència disponible sobre aquest tema en adolescents és limitada.

Tradicionalment, l'estudi de la psicopatologia s'ha centrat en concepcions lineals de la conducta humana. En resposta a això, la Teoria dels Sistemes Dinàmics (TSD), una perspectiva recent dins l'àmbit de la psicologia, pot ser útil a l'hora d'incrementar el nostre coneixement sobre la conducta humana com el que és: un fenomen complex i no lineal.

L'objectiu principal d'aquesta tesi va ser emprar la TSD com a marc teòric per a donar resposta a algunes de les llacunes existents sobre la vulnerabilitat psicològica i fisiològica per al desenvolupament de TIs en adolescents. Es va intentar donar resposta a dues preguntes generals: a) Es pot distingir entre adolescents sans més i menys vulnerables a desenvolupar TIs, mitjançant l'ús d'índexs de complexitat afectiva i complexitat cardíaca?, b) Com es relacionen la complexitat afectiva i cardíaca dels adolescents sans amb altres factors de vulnerabilitat per als TIs ja establerts, com el sexe, els símptomes internalitzants o la desregulació emocional?

Es van dissenyar cinc estudis sota condicions ecològiques o de laboratori, amb l'objectiu d'obtenir una millor representació de les dinàmiques afectives i cardíaques. En l'estudi 1, una mostra d'adolescents sans va informar sobre els seus nivells d'estat d'ànim, ansietat i preocupació, dues vegades per dia durant un període de 100 dies. Els estudis 2 i 3 van consistir en l'enregistrament de l'activitat cardíaca d'adolescents sans durant 120 minuts mentre duien a terme les seves activitats diàries dins el context acadèmic. La mostra de l'estudi 2 es va dividir en dos grups en funció del sexe (nins/nines) i del nivell d'ansietat (alt/baix). Per a l'estudi 3 es va seleccionar una mostra aleatòria, independent del nivell d'ansietat dels participants. En els estudis 4 i 5 es va enregistrar la resposta cardíaca d'adolescents sans mentre es sotmetien a un protocol d'inducció d'estrès social. L'estil de regulació emocional dels participants també es va avaluar durant l'estudi 4.

Quasi tots els exponents d'escala varen demostrar la seva fractalitat i multiestabilitat. A més a més, els exponents de preocupació correlacionaren positivament amb el control intencional, i negativament amb l'afectivitat negativa i la necessitat

d'afiliació (estudi 1). En referència a la complexitat cardíaca, es va trobar que aquesta era més baixa en les nines en comparació amb els nins (estudis 2, 3 i 5), així com en aquells adolescents amb una major tendència a emprar estratègies de regulació emocional més negatives en general, però només quan passaren de la fase d'estrès a la de recuperació (estudi 4). També es va observar que a menor complexitat cardíaca, major nivell de símptomes internalitzants (estudi 3). Finalment, el sexe femení va predir una menor complexitat cardíaca, al contrari de l'estil de regulació emocional negatiu, que es va trobar que estava positivament relacionat amb la complexitat cardíaca (estudi 4).

En resum, aquesta tesi doctoral demostra que les fluctuacions afectives i cardíaques es troben sota processos de regulació complexos amb memòria, que tenen en compte la informació de diferents escales temporals per assegurar una adaptació més exitosa a la vida diària. També es conclou que aquells adolescents més vulnerables a desenvolupar un TI (nines, majors símptomes internalitzants o estratègies de regulació emocional disfuncionals) semblen tenir menors nivells de complexitat afectiva i cardíaca que aquells adolescents menys vulnerables. Per tant, una complexitat/flexibilitat afectiva i cardíaca reduïdes podrien constituir marcadors psicològics i fisiològics d'un patró desadaptatiu a l'hora de confrontar demandes internes i externes.

Resumen

Los trastornos internalizantes (TIs) son las psicopatologías más prevalentes en adultos y generan un gran deterioro en muchas áreas de la persona y de sus familiares. La edad media de inicio de muchos de estos trastornos se encuadra dentro de la adolescencia, motivo por el cual esta etapa se considera un periodo de riesgo para el desarrollo de TIs. La probabilidad de que un TI se mantenga de la adolescencia hasta la edad adulta es elevada, ya que estos problemas no son suficientemente detectados por los sistemas de atención primaria. En este sentido, el estudio de los factores de vulnerabilidad relacionados con los TIs puede ayudar esclarecer la génesis y el mantenimiento de estos trastornos y, consecuentemente, ayudar a diseñar programas de prevención y de intervención basados en la evidencia empírica. Por lo que sabemos, la evidencia disponible sobre este tema en adolescentes es limitada.

Tradicionalmente, el estudio de la psicopatología se ha centrado en concepciones lineales de la conducta humana. En respuesta a ello, la Teoría de los Sistemas Dinámicos (TSD), una perspectiva reciente dentro del ámbito de la psicología, puede ser útil a la hora de incrementar nuestro conocimiento sobre la conducta humana como lo que es: un fenómeno complejo y no lineal.

El objetivo principal de esta tesis fue utilizar la TSD como marco teórico para dar respuesta a algunas de las lagunas existentes sobre la vulnerabilidad psicológica y fisiológica para el desarrollo de TIs en adolescentes. Se intentó dar respuesta a dos preguntas generales: a) ¿Se puede distinguir entre adolescentes sanos más y menos vulnerables a desarrollar TIs, mediante el uso de índices de complejidad afectiva y cardíaca?, b) ¿Cómo se relacionan la complejidad afectiva y cardíaca de los adolescentes sanos con otros factores de vulnerabilidad para los TIs ya establecidos, como el sexo, los síntomas de ansiedad o la desregulación emocional?

Se diseñaron cinco estudios en condiciones ecológicas o de laboratorio con el objetivo de obtener una mejor representación de las dinámicas afectivas y cardíacas. En el estudio 1, una muestra de adolescentes sanos informó sobre sus niveles de estado de ánimo, ansiedad y preocupación, dos veces al día durante un periodo de 100 días. Los estudios 2 y 3 consistieron en registrar la actividad cardíaca de adolescentes sanos durante 120 minutos mientras llevaban a cabo actividades diarias dentro del contexto académico. La muestra del estudio 2 se dividió en dos grupos en función del sexo (chicos/chicas) y del nivel de ansiedad (alto/bajo). Para el estudio 3 se seleccionó una muestra aleatoria, independiente del nivel de ansiedad de los participantes. En los estudios 4 y 5 se registró la respuesta cardíaca de adolescentes sanos mientras se sometían a un protocolo de inducción de estrés social. El estilo de regulación emocional de los participantes también se evaluó en el estudio 4.

Casi todos los exponentes de escala demostraron su fractalidad y multiestabilidad. Además, los exponentes de preocupación correlacionaron positivamente con el control

intencional, y negativamente con la afectividad negativa y la necesidad de afiliación (estudio 1). En referencia a la complejidad cardíaca se encontró que ésta era inferior en las chicas en comparación con los chicos (estudios 2, 3 y 5), así como en aquellos adolescentes con una mayor tendencia a utilizar estrategias de regulación emocional negativas en general, pero solo cuando pasaron de la fase de estrés a la de recuperación (estudio 4). También se observó que, a menor complejidad cardíaca, mayor nivel de síntomas internalizantes (estudio 3). Finalmente, el sexo femenino predijo una menor complejidad cardíaca, al contrario que el estilo de regulación emocional negativo, que se observó que estaba positivamente relacionado con la complejidad cardíaca (estudio 4).

En resumen, esta tesis doctoral demuestra que las fluctuaciones afectivas y cardíacas se encuentran bajo procesos de regulación complejos con memoria, que tienen en cuenta la información de diferentes escalas temporales para asegurar una adaptación más exitosa a la vida diaria. También se concluye que aquellos adolescentes más vulnerables a desarrollar un TI (chicas, mayores síntomas de ansiedad o estrategias de regulación emocional disfuncionales) parecen tener menores niveles de complejidad afectiva y cardíaca que aquellos adolescentes menos vulnerables. Por tanto, una complejidad/flexibilidad afectiva y cardíaca reducidas podrían constituir marcadores psicológicos y fisiológicos de un patrón desadaptativo a la hora de confrontar demandas internas y externas

I. Background and general framework

1. Internalizing problems: anxiety and depression

Depressive and anxiety disorders are included in a wider category called internalizing disorders (IDs). The terms "internalizing" and "emotional" disorders are considered synonyms, but the former has been typically used for child and adolescent psychopathology (Kovacs & Devlin, 1998). The use of the broad term "ID" is supported by empirical evidence that shows the great overlap between anxiety and depression in terms of high comorbidity, similar symptomatology or common vulnerability factors (Balázs et al., 2013; David Harrison Barlow, 1991, 2002; Canals, Voltas, Hernández-Martínez, Cosi, & Arija, 2019; Clark & Watson, 1991; Craske, 2003; Kessler et al., 2005; Ormel et al., 2015). For these reasons, many authors are making efforts toward a unified consideration of anxiety and depressive disorders and the vulnerability factors associated (e. g. Barlow et al., 2017; Craske, 2012). These conditions show the highest prevalence amongst psychopathological disorders in adults (Kessler et al., 2005). According the National Comorbidity Survey, in the USA there is a global prevalence of 28.8% for anxiety disorders. For depression disorders, the National Comorbidity Survey points to a global prevalence of 20.8%. In Spain, the global prevalence has been situated in 9.3% for anxiety disorders, whereas in 11.4% for depressive disorders (Haro et al., 2006). The presence of IDs generates a great impairment in several areas of the individual and their relatives (Angermeyer, Kilian, Wilms, & Wittmund, 2006; Joffe et al., 2012; Mendlowicz & Stein, 2000; Pinto-Meza et al., 2009; Wittmund, Wilms, Mory, & Angermeyer, 2002), and results in high direct and indirect economic costs for public health all over the world (Bandelow & Michaelis, 2015; Kessler, 2012; Lynch & Dickerson, 2018).

1.1. The importance of adolescence

Adolescence is a developmental period, highly changeable from a neurobiological, behavioral and psychosocial perspective (Hollenstein & Lougheed, 2013). All these changes lead to innumerable affective situations where a successful management of emotions is necessary for an adaptive functioning. It is well-established that adolescence marks the median age of onset for many IDs (Essau, Lewinsohn, Olaya, & Seeley, 2014; Goldman, 2012; Kessler et al., 2005), thus it is considered a risk period for their development. The presence of internalizing problems can interfere with academic achievement and interpersonal relationships, increasing suicide risk and the manifestation of other psychopathological conditions (e. g. Essau et al., 2014; Kessler, 2012; Saveanu & Nemeroff, 2012). Many of the adolescents diagnosed with an ID present one or more comorbid conditions (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). It is specifically relevant the high comorbidity between both anxiety and depression (Merikangas et al., 2007; Merikangas et al., 2010). Contrary to adolescents with

externalizing problems, who manifest clearly visible disruptive behaviors, adolescents with internalizing problems can usually go unnoticed for a long period of time. For instance, in the case of anxiety, clinical data show that only a low percentage (21%) of adolescents with anxiety disorders is referred to mental health centers for these problems, which may indicate that these conditions are not sufficiently detected in primary care or school settings (Olofsdotter, Vadlin, Sonnby, Furmark, & Nilsson, 2016). Once the ID is detected, a small percentage of the adolescents will receive treatment, and not all of them will finish it successfully (Essau, 2005; Farrell & Barrett, 2007). All this contributes to the maintenance of these disorders from adolescence to adulthood (Costello et al., 2003).

1.2. Vulnerability factors for internalizing disorders

Even though the vast majority of research regarding pathogenesis of IDs has been traditionally focused on adults, relatively robust theories regarding the vulnerability for IDs in children and adolescents already exist (e.g. Lonigan, Vasey, Phillips, & Hazen, 2004; Rothbart, 2007; Weems, 2008). However, there are still inconclusive results regarding the etiology and the related vulnerability factors of these disorders in adolescents (see for instance, Beidel & Alfano, 2011). This lack of information will be further reviewed in the present introduction.

An important question is why under the same conditions some individuals manifest a psychopathological disorder whereas others never do. Nowadays, everybody takes for granted the implication of vulnerability factors in the etiology of mental disorders. The American Psychological Association (APA), defines a vulnerability factor as "any variable that, if triggered or experienced, affects the probability of an individual to develop a condition, disease or disorder. The study of related vulnerability factors can prove insight into the genesis and the maintenance of IDs and, consequently, can help to design empirically based programs for prevention and intervention against these conditions" (APA, 2019).

Several factors (e.g. personality and temperamental traits, altered autonomic flexibility, anxiety and depressive symptomatology, etc.) have been proposed as vulnerability factors for the developing of IDs (e. g. Aldao, Nolen-Hoeksema, & Schweizer, 2010; Balázs et al., 2013; Balzarotti, Biassoni, Colombo, & Ciceri, 2017; David Harrison Barlow, 1991, 2002; Beauchaine & Thayer, 2015; Craske, 2003; Eisenberg, Spinrad, & Eggum, 2010; Essau, Lewinsohn, Lim, Ho, & Rohde, 2018; Goldman, 2012; McLean, Asnaani, Litz, & Hofmann, 2011; Rothbart & Bates, 2006; Thayer & Lane, 2009). Most of these factors are embedded into diathesis-stress models for the development of anxiety and depressive disorders (e. g. David Harrison Barlow, 1991, 2002; Craske, 2003). For the sake of synthesis, only the vulnerability factors targeted in the current doctoral thesis will be further described in the following sections.

1.2.1. The presence of subthreshold internalizing symptoms

The majority of the studies aimed at disentangling the pathogenesis of IDs are focused on individuals who already suffer from an ID. Individuals who do not present a full-blown disorder (they do not fulfil all the required DSM or ICD criteria for a particular disorder) but suffer from subthreshold symptoms, have usually been overlooked in scientific research. However, there is evidence that these adolescents present similar prevalence rates, levels of distress and impairment than adolescents diagnosed with a full-blown disorder (Balázs et al., 2013; Lewinsohn, Shankman, Gau, & Klein, 2004). Furthermore, according to several authors, the presence of anxiety or depression symptoms is one of the highest predictors of developing an ID in the future (Balázs et al., 2013; Essau et al., 2018; Fergusson, Horwood, Ridder, & Beautrais, 2005; Shankman et al., 2009) and the combination of both types of symptoms has shown the greater risk for presenting a future ID (Karsten et al., 2011).

Taking all this into consideration, subclinical symptoms may be considered conditions quantitatively lower than full-blown disorders, though not qualitatively distinctive (Shankman et al., 2009). A dimensional approach that contemplates anxiety or depression not as discrete entity, but as continuum of symptoms, should be considered for a better understanding of the etiology of these conditions (Balázs et al., 2013; Karsten et al., 2011). Thus, adolescents with high levels of anxiety and/or depression, could be considered as adolescents "at-risk" for the later appearance of these disorders and might represent a good target for early detection and prevention (Fergusson et al., 2005; Shankman et al., 2009; Wolitzky-Taylor et al., 2014).

1.2.2. Temperament and emotion regulation

Within the field of development psychopathology, reactive and regulatory aspects of temperament and emotion dysregulation have been pointed out as important predictors of IDs development and maintenance (Berking & Wupperman, 2012; Craske, 2003; Hervás & Vázquez, 2006; Kovacs, Joormann, & Gotlib, 2008; Rothbart & Bates, 2006). As pointed out by the leading authors of the field, the study of temperament, emotion regulation and their psychobiological correlates, in relation to psychopathology are inseparable (Beauchaine, 2001; Nigg, 2006; Porges, 1995).

1.2.2.1. Temperament

From early childhood, infants show variability in their reactions to contextual demands. These reactions and the mechanisms used to regulate them constitute the temperament of the child (Rothbart & Bates, 2006). Temperament is biologically based, arises from the genetic heritage and manifests itself in the adult personality (Caspi et al., 2003; Posner, Rothbart, & Sheese, 2007). Rothbart (2007) proposed a temperament model that supports the difference between a reactive and a regulatory temperament.

According to the same author, "temperament is defined as individual differences in emotional, motor, and attentional reactivity measured by latency, intensity, and recovery of response and self-regulation processes such as effortful control that modulate reactivity" (p. 207). Available evidence claims that temperamental characteristics are importantly related with the individual adjustment and the development of internalizing problems.

Within the reactive temperament, negative affectivity is the factor most frequently associated with the onset and development of IDs, as well as with higher levels of anxious-depressive symptomatology (e.g. Barlow, 1991, 2002; Craske, 2003; Lonigan et al., 2004; Nigg, 2006). Negative affectivity is the tendency of the defensive motivational systems (i.e. the behavioral inhibition system) to hyperreact, increasing the probability of experiencing negative emotions, such as sadness, fear, blame, hostility, in a wide range of situations (Craske, 2003).

The capacity of effortful control has been considered the central factor within the regulatory temperament. Effortful control is described as the capability to focus and shift attention, as well as to inhibit a dominant response and/or initiate a subdominant response (Rothbart & Rueda, 2005). Several authors have reported diminished effortful control abilities in children and adolescents with internalizing symptoms or with high probabilities of experience an ID, interpreting these results as an increased vulnerability to IDs (Eisenberg et al., 2010; Muris & Meesters, 2009; Muris & Ollendick, 2005; Nigg, 2006; Oldehinkel, Hartman, De Winter, Veenstra, & Ormel, 2004; Sportel, Nauta, de Hullu, & de Jong, 2013; Sportel, Nauta, de Hullu, de Jong, & Hartman, 2011). On the other hand, effortful control and negative affectivity are related in a way that the first moderates the effect of latter, i.e. children with high negative affectivity would show less psychological problems if they also have higher effortful control (Rothbart & Bates, 2006; Rothbart, Posner, & Kieras, 2006).

In addition to negative affectivity and effortful control, there are two other temperament constructs proposed by Rothbart: surgency/extraversion and affiliativeness. Both constructs, together with negative affectivity, would conform the reactive part of temperament. Surgency or extraversion refers to the tendency to seek and enjoy experiences of high intensity, with reduced emotions of shyness and fear. Low levels of surgency may lead to internalizing symptoms in adolescents (Oldehinkel et al., 2004). Affiliativeness is defined as the desire of closeness with others and the tendency to be responsive to others. Affiliativeness has been found to predict both low externalizing and high internalizing problems in adolescents (Ormel et al., 2005).

1.2.2.2. Emotion regulation

The field of emotion regulation (ER) is one of the areas that is growing fastest in psychology. Despite this increment in productivity, a consensual definition of ER does not exist yet and many terms have been used to refer emotion regulation processes (e. g.

Bridges, Denham, & Ganiban, 2004; Eisenberg & Spinrad, 2004). Many authors agree that the term "emotion regulation" involves all the cognitive and behavioral strategies that an individual uses to modulate its emotional experience, considering the evaluative-affective, behavioral and physiological domain (Bridgett, Burt, Edwards, & Deater-Deckard, 2015; Gross & Thompson, 2007). These processes constitute the individual pattern of response of each person to contextual demands (Aldao, 2013) and are highly influenced by temperamental factors (Eisenberg et al., 2010). In fact, the presence of negative affectivity has been related with the proneness to display dysfunctional emotion regulation (ER) strategies. Specifically, negative affectivity would promote the election of ER strategies such as rumination or worry (e.g. Messerli-Bürgy et al., 2012; Tortella-Feliu, Balle, & Sesé Albert, 2010; Verstraeten, Vasey, Raes, & Bijttebier, 2009). On the other hand, reduced effortful control abilities have also been found in individuals with a tendency to engage in dysfunctional ER strategies (Eisenberg et al., 2010; Tang et al., 2007).

The adaptive management of our emotions is essential for our psychological well-being and social functioning (Aldao et al., 2010; Balzarotti, Biassoni, Villani, Prunas, & Velotti, 2016; Eisenberg et al., 2010; Gross, 1998). Deficits in self-regulatory capabilities have been extensively related to a wide range of social and psychopathological problems, including internalizing problems (e.g. Aldao et al., 2010; Barlow, Allen, & Choate, 2004; Eisenberg et al., 2010; Ladouceur et al., 2005; McLaughlin, Hatzenbuehler, Mennin, & Nolen-Hoeksema, 2011; Silk, Steinberg, & Morris, 2003; Trosper, Buzzella, Bennett, & Ehrenreich, 2009). There is also consensus that exhibiting emotion dysregulation in the face of a negative event is an important predictor of IDs development later in life (Hervás & Vázquez, 2006; Kovacs et al., 2008). On the other hand, it is known that ER abilities are continuously developed through adolescence, since adolescents show less ER skills than adults (Garnefski & Kraaij, 2006; McRae et al., 2012). The development of effective ER abilities is essential during adolescence, since there is an increase of the perception of stress and daily hassles (Larson & Ham, 1993; Seidman, Allen, Aber, Mitchell, & Feinman, 1994), but also of the real presence of stressful events (Spear, 2009). Adolescents have to cope with daily stressors necessitating adaptive responses in the physiological, cognitive, and behavioral domains. There is specific evidence that the engagement in adaptive ER strategies helps to mitigate maladaptive responses when faced with stress (Moriya & Takahashi, 2013; Vanderhasselt et al., 2014). Therefore, self-regulation in the face of stressors and negative emotions has profound implications for adolescents' long-term well-being and risk of psychopathology (Asselmann, Wittchen, Lieb, Höfler, & Beesdo-Baum, 2016; Compas et al., 2017; Spear, 2009).

From childhood to adolescence, the type of coping typically used increases and shifts from more behaviorally orientated strategies to more internal, cognitive strategies (Aldwin, 1994). Aldao and Nolen-Hoeksema (2010) have defined cognitive ER as "cognitive responses to emotion-eliciting events that consciously or unconsciously attempt to modify the magnitude and/or type of individuals' emotional experience or the event itself" (p. 974). There are several cognitive strategies to regulate emotions (see Gross, 1988 for a review). The Cognitive Emotion Regulation Questionnaire (CERQ) developed by Garnefski, Kraaij, and Spinhoven (2001) distinguishes between 9 types of cognitive ER strategies: rumination, catastrophizing, self-blame, other-blame, positive refocusing, positive reappraisal, planning, acceptance and putting into perspective.

Traditionally, cognitive ER strategies have been divided in two categories, regarding their functionality. In one group, we would have the positive or adaptive ER strategies, whereas in the other group we find the negative or maladaptive ER strategies (Aldao et al., 2010; Garnefski et al., 2001; Gross, 2015). The use of these strategies usually depends on the context, but there seems to be an individual dispositional trend or style in the greater use of adaptive or maladaptive strategies (Garnefski et al., 2001; Jermann, Van Der Linden, D'Acremont, & Zermatten, 2006). Furthermore, there is evidence that the maladaptive ER strategies are not so affected by contextual factors as the positive strategies (Aldao & Nolen-hoeksema, 2012). According to Garnefski et al. (2001) the adaptive strategies would include positive refocusing, positive reappraisal, planning, acceptance and putting into perspective. These strategies have been negatively related to anxiety and depressive symptoms in adolescents, so that the higher the use of adaptive strategies, the lower the symptoms (see Schäfer, Naumann, Holmes, Tuschen-Caffier, & Samson, 2017, for a meta-analytic review). On the other hand, the maladaptive ER strategies would include rumination, catastrophizing, self-blame, or others-blame (Garnefski et al., 2001). The predominant use of these strategies have also been related to the onset and maintenance of anxiety and depression problems in youths, being the use of maladaptive ER strategies positively correlated to the presence of internalizing problems (Cisler, Olatunji, Feldner, & Forsyth, 2010; Garnefski & Kraaij, 2016; Garnefski et al., 2001; Garnefski, Rieffe, Jellesma, Terwogt, & Kraaij, 2007; see Schäffer et al., 2017 for a review) and how they cope with stressful events (Brosschot, Gerin, & Thayer, 2006; Brosschot, Verkuil, & Thayer, 2010).

The vast majority of studies have been focused on investigating single ER strategies. However, psychopathology "cannot be traced to one specific emotion regulation strategy, but to a combined 'play' of various strategies" (Garnefski et al., 2001, p. 1325), so we should embrace the concept of ER "style". Certainly, a sharp distinction between adaptive and maladaptive ER styles cannot be made because individuals use specific strategies depending on the context, but considering patterns or styles may contribute important knowledge about associations between ER and psychopathology.

On top of all this, emotionality and emotion regulation are manifested across multiple systems, including behavioral responses, subjective experiences and physiological changes (Tracy, Klonsky, & Proudfit, 2014). Therefore, following the Research Domain Criteria (RDoC), Beauchaine & Thayer (2015) recommend the study of emotion dysregulation in children and adolescents at multiple levels of analysis, embracing behavioral and biological domains amongst others.

1.2.3. Cardiac vagal tone

Psychophysiology research has extensively focused on identifying biomarkers of ER, since changes in physiological activation represent a main emotional response domain (see Balzarotti et al., 2017, for a review; Tracy et al., 2014). Self-regulation

emotional processes are widely influenced by the autonomous nervous system (ANS), whose activity is reflected by the cardiac response.

The polyvagal theory exposed by Porges (1995) is an effort to link the ANS's activity with behavior, and offers a plausible explanation of social, emotional and communicative behaviors, as well as their possible related disturbances. According to this theory, the vagus nerve is the main nerve of the parasympathetic branch of the ANS and has an important role dampening the activity of the sympathetic branch of the ANS. On the one hand, the vagus nerve acts as a break, inhibiting the acceleratory innervations of the heart by the sympathetic nervous system in situations of social or attentional demands. In these situations, a higher vagal tone is expected and the heart rate is reduced as a result. On the other hand, the vagus nerve can also withdraw the inhibitory capacity in fight or flight situations, which would result in a low vagal tone and consequently, an increase of heart rate. The synergy between these two mechanisms allows for a rapid change in the visceral state, increasing or decreasing HR, depending on contextual demands.

Cardiac vagal tone is reflected in heart rate variability (HRV) and is one of the most studied physiological markers of psychopathological problems where emotion dysregulation is present (Balzarotti et al., 2017). HRV is defined as the variations in the length of successive interbeat intervals (IBIs, Task Force of the European Society of Cardiology, 1996). There are different ways to measure HRV and there is still no consensus about which one better reflects it. In fact, we must take into consideration that HRV is not a unitary concept and every measure will capture different properties.

HRV can be calculated using time domain measures by quantifying the length of successive intervals, such as the average number of heartbeats per unit of time (heart rate) or the standard deviation of NN intervals (SDNN). One of the most frequently used measures within the time domain is the squared root of the mean of the squared successive differences between adjacent NN intervals (RMSSD). This index account for the influence of the parasympathetic system on the heartbeat. It has proven to be reliable for the assessment of stress levels in short-term analysis (Pereira, Almeida, Cunha, & Aguiar, 2017) and for analyses with adolescent samples (Weiner & McGrath, 2017). Another widely used measure is the respiratory sinus arrhythmia (RSA), which reflexes HRV over the respiration cycle. It is considered an index of vagally-mediated HRV. Over the past decades, RSA has been established as a reliable peripheral biomarker of emotion regulation (Beauchaine, 2015).

Measures from the time domain do not give information about the sources of variability, i.e. we cannot know the underlying mechanisms of the ANS (sympathetic or parasympathetic) that cause HRV changes. For that purpose, frequency domain measures of HRV are used. These measures are derived from the decomposition of heartbeat fluctuations into power of main frequency components. Low frequency (LF, 0.4–0.15Hz) band power has traditionally been interpreted as an index of sympathetic cardiac control. However, recent studies challenge this interpretation and suggest that the LF seems to be a mix of sympathetic, parasympathetic, and other unidentified factors (Billman, 2013). High frequency (HF, 0.15– 0.40Hz) band power is widely considered an index of vagally-

mediated HRV in resting conditions, i.e. the variability that depends on the inhibitory action of the ANS's parasympathetic branch. HF power and RMSSD are highly correlated, but the former is less influenced by respiratory activity than the latter (Laborde, Mosley, & Thayer, 2017).

Time and frequency domain measures are considered linear measures and despite that they provide relevant information about the cardiovascular system's activity, there are several underlying mechanisms that cannot be captured by these traditional methods. As a small foretaste, the use of nonlinear measures can help to complete the whole picture by providing information about the irregularity and complexity of the heartbeat. This new approach will be further discussed in the second and third section of the present introduction.

1.2.3.1. Heart rate variability and emotion regulation

As previously stated, there are well-established psychobiological theoretical models that associate a diminished HRV (or reduced vagal tone) with emotion dysregulation problems and a lack of behavior and autonomic flexibility in children, adolescents and adults (Beauchaine, 2001; Beauchaine & Thayer, 2015; Porges, 1995; Julian F. Thayer & Lane, 2000; Julian F Thayer & Lane, 2009). These models have been proposed to describe neural pathways between brain and heart, providing a framework to conceptualize cardiac vagal control as a biomarker of ER. Specifically, Balzarotti et al. (2017) reviewed the literature on resting cardiac vagal control and phasic cardiac vagal changes in adults. This review shows that high resting vagal tone is associated with the use of adaptive ER strategies and more flexible emotional responding, and concludes that resting cardiac vagal activity is an objective biomarker of ER. Regarding phasic changes, decreases in vagal control have been observed in response to stress, whereas vagal control increases have been related to recovery from stress or self-regulatory efforts. Vagal withdrawal per se is not maladaptive, as the increment in physiological reactivity may aid youths to respond adaptively to the challenges of adolescence. The problem is when vagal reduction results in stress dysregulation (e. g. vagal control is too slowly re-established during recovery from stress) amongst adolescents at risk, thus probably increasing further their vulnerability for psychopathology (Spear, 2009).

There are studies that relate some specific adaptive and maladaptive ER strategies with cardiac adjustment when confronting stressful situations in laboratory settings. For instance, Brosschot and colleagues (2010; 2006) formulated the perseveration cognition hypothesis and considered rumination as a core component. Ottaviani et al. (2016) suggested that perseverative cognition may contribute to impaired psychological and somatic health by expanding the duration of physiological activation to stressors beyond the reactivity period, also including anticipation and recovery. In the same vein, Aldao, McLaughlin, Hatzenbuehler, and Sheridan (2014) reported in a sample of 157 adolescents that rumination might be specifically associated with physiological recovery from stress, but not with physiological reactivity. Some studies have also reported that acceptance strategy is related to lower physiological stress reactivity in healthy adults (e. g. Lindsay, Young, Smyth, Brown, & Creswell, 2018; Paul, Stanton, Greeson, Smoski, & Wang,

2013). All this evidence is focused on separate ER strategies, but individuals do not usually use only one single strategy, but a combined interplay of them (Garnefski, Legerstee, Kraaij, Van Den Kommer, & Teerds, 2002). Similar to rumination, a HRV suppression (i.e. lower vagal tone) was found during stress in adults with general ER difficulties (Berna, Ott, & Nandrino, 2014). However, whether positive or negative general ER styles affect cardiac reactivity and recovery in stress conditions remains far from clear, especially in adolescents.

1.2.3.2. Heart rate variability and internalizing problems

Recently, Beauchaine and Thayer (2015) discussed the role of HF-HRV as a transdiagnostic biomarker of mental illness. In adults, it is well-established that a lower vagal tone (assessed by both time and frequency measures) in resting conditions is related to the presence of anxiety and depression disorders (for a review see Chalmers, Quintana, Abbott, & Kemp, 2014; Kemp et al., 2010). Regarding temporal sequencing, a longitudinal study suggested that altered cardiac vagal tone might be preceding the development of internalizing problems, such as depression (Jandackova, Britton, Malik, & Steptoe, 2016). Furthermore, techniques aimed at enhancing HRV, such as HRV biofeedback, have proven clinically significant effects on the treatment of IDs (Goessl, Curtiss, & Hofmann, 2017; Karavidas et al., 2007), thus supporting the role of cardiac vagal tone as a biomarker for emotion dysregulation related disorders.

Likewise, the available evidence in children and adolescent seems to indicate that individuals with internalizing problems display lower resting HRV than their healthy counterparts. Henje Blom, Olsson, Serlachius, Ericson, and Ingvar (2010) reported lower HRV in adolescent females with an anxiety disorder compared to a healthy control group of females. Other studies have demonstrated that anxiety and depression are related to cardiac functioning in adolescents even though not reaching clinical levels. For instance, in Balle, Tortella-feliu, and Bornas (2013), adolescents at risk for anxiety disorders presented lower HF across different experimental conditions. On the other hand, Dietrich et al. (2007) found that internalizing problems in healthy adolescents were associated with higher heart rate and lower RSA at resting conditions. These disorders have also been related to altered cardiac responses to stress in children and adolescents (Pang & Beauchaine, 2013; Schmitz, Krämer, Tuschen-Caffier, Heinrichs, & Blechert, 2011).

1.2.4. Ecological vs laboratory conditions

Most of the studies commented in the previous section calculated HRV measures on short electrocardiogram (ECG) recordings in laboratory settings (resting state or stressful task condition). Despite the great value of these results (e. g. high level of control), data derived from laboratory settings are far from representing adolescents' everyday life conditions and their ecological validity and generalization can be questioned (see for instance, Barry, Frick, & Kamphaus, 2013). Some studies have recorded cardiac activity for a longer period of time (usually 24 hours) in order to

investigate differences in HRV between day and night. However, during the day, activities with different emotional loads take place, and therefore HRV measures of 24-hour recordings reflect the mean (nonspecific) cardiac regulation. Studies of ecological recordings that represent cardiac regulation during specific and meaningful everyday conditions are still scarce and have led inconsistent results (e.g. Bobkowski et al., 2017; Faulkner, Hathaway, & Tolley, 2003; Umetani, Singer, McCraty, & Atkinson, 1998; Yukishita et al., 2010). Some of these will be presented in the next section of this introduction. As adolescents are engaged in school activities for several hours every day, recordings taken in regular school settings when they perform academic tasks, can provide ecological and meaningful knowledge about their everyday hear rate regulation (see Bornas, Balle, De la Torre-Luque, Fiol-Veny, & Llabrés, 2015; De la Torre-Luque, Fiol-Veny, Balle, & Bornas, 2016).

1.2.5. Sex differences

The sex of the individual has been widely related to the presence of IDs. In particular, it has been observed that adult females are more prone to develop anxiety- and depression-related disorders than adult males (Goldman, 2012; McLean et al., 2011). Data from prevalence studies conducted with Spanish population (Alonso et al., 2004; Haro et al., 2006) confirm the fact that females have higher rates of anxiety and depression disorders. Many factors, from sociocultural rules and education patterns to temperamental or physiological sex differences in neurovisceral regulation systems, can help explain this fact (Barlow, 2000; Yap, Pilkington, Ryan, & Jorm, 2014). In adolescents, there are also studies showing a greater incidence of IDs for females in comparison to males, (Merikangas et al., 2010; Zahn-Waxler, Shirtcliff, & Marceau, 2008), more comorbidity and both homotypic and heterotypic continuity (Costello et al., 2003). Hence, female sex emerges as a marker of vulnerability for the development of internalizing problems (e.g. Beesdo, Knappe, & Pine, 2009; Noble, 2005).

1.2.5.1. Sex and heart rate variability

Since adolescence is the mean age of onset of many IDs (Essau et al., 2014; Goldman, 2012; Kessler et al., 2005), it is worth asking whether there exist sex differences in HRV in this developmental stage. Since internalizing problems have been related to reduced HRV in resting conditions on the one hand (Chalmers et al., 2014; Kemp et al., 2010), and the female sex on the other (Goldman, 2012; McLean et al., 2011), a diminished HRV at rest would be expected for adolescent females. Furthermore, it is necessary to point out that heart rate regulation is influenced by several brain areas (Julian F Thayer & Lane, 2009), which have been proven to be structural and functionally different between male and female adolescents (Lenroot & Giedd, 2010). If all this were true, adolescent females could be more physiologically vulnerable to IDs than males. This would not imply a causal relationship between a less variable or flexible regulation of the heart beat and the internalizing symptoms, but some underlying common causal factors (e.g. in the central nervous system) that would result in internalizing problems and lower HRV.

A recent meta-analysis (Koenig, Rash, Campbell, Thayer, & Kaess, 2017) confirmed that adolescent females display lower vagal activity and higher mean heart rate than adolescent males, during resting short-term recordings. Therefore, females show a less flexible autonomic response than males, at least under resting conditions. Although still inconclusive, studies with longer cardiac recordings (i.e. 24h) have found results in a similar way. For instance, Faulkner et al. (2003) found lower SDNN values for adolescent females in comparison to males, but no sex differences in HF power. Silvetti, Drago, and Ragonese (2001) calculated several time domain measures of HRV and also found lower SDNN in females recordings from children and adolescents (1–20 years old), though no sex differences were found in other measures (e.g., RMSSD). However, Bobkowski et al. (2017) did not find sex differences in HRV measures from children and adolescents (aged 3–18 years).

Studies with adult samples, however, have found that females display greater levels of cardiac vagal control than males (see Koenig & Thayer, 2016) for a meta-analytical review). That seems to be contradictory with the results reported in adolescents, but studies on short-term and long-term HRV differences across age groups (Abhishekh et al., 2013; Umetani et al., 1998) can help to disentangle this discrepancy. Interestingly, Moodithaya and Avadhany (2012) performed 5-min recordings and found that, although not statistically significant, girls had lower HF power than boys in the group of 12 to 19-year-old adolescents, but this difference turned out to be inverted in the 20 to 40-year-old adult group. These findings highlight a lack of stability in cardiac features throughout the lifespan. Hence, the study of these features across different maturational stages, specifically in adolescence, becomes crucial.

Results of sex differences from studies with experimentally induced stress are less consistent. The Trier Social Stress Test for children (TSST-C; (Buske-Kirschbaum et al., 1997), is a protocol to induce low-to-moderate psychological stress under laboratory settings. Within this protocol, a social-evaluative stimulus that is deemed challenging, threatening, and unexpected has to be faced. The TSST-C is one of the most widely used protocols in this area (for a review see Allen, Kennedy, Cryan, Dinan, & Clarke, 2014). Using this protocol, Kudielka, Buske-Kirschbaum, Hellhammer, and Kirschbaum (2004) reported sex differences in children and younger adults, but not in elderly adults. Females displayed higher heart rate increases during stress exposure than males. Besides, Hamilton and Alloy (2016) reviewed studies on HRV-reactivity and stress in community samples, finding a lack of sex differences in HRV-reactivity for adults and too few studies to conclude for adolescents. Thus, sex differences in heart rate and HRV could exist in children and early adolescents but disappear in late adolescence and adulthood. How the adolescents perceive the stressor is also important to consider, because it can influence their reactions to the situation. For instance, Jamieson, Mendes, and Nock (2013) found that adolescents who were trained to reappraise their arousal showed more adaptive cardiovascular responses to stress. In this sense, some authors found that adolescent females perceive interpersonal events as more stressful than males (Hampel & Petermann, 2006) and report higher levels of interpersonal stress (Moksnes, Moljord, Espnes, & Byrne, 2010).

So far, we have reviewed the empirical evidence that relates HRV with sex on one side and HRV with internalizing symptoms on the other. Some authors have combined the study of sex, anxiety problems and HRV by using short-term ECG recordings, and have reported interesting results. For instance, Henje Blom et al. (2010) found lower HRV by means of reduced SDNN, HF and LF power in adolescent females with anxiety disorders in comparison to a healthy control group of females. Additionally, Greaves-Lord et al. (2010) found that low RSA reactivity predicted anxiety levels in healthy adolescent females 2 years later, but not in males. On the other hand, Greaves-Lord et al. (2007) reported that low RSA was related to self-reported anxiety problems, but only in boys. None of these studies analyzed the interaction between sex and anxiety problems, even though current evidence points to important relationships between both of them and several heart rate regulation properties.

2. Dynamic systems theory

The Dynamic System Theory (DST) is a recent perspective in the field of Psychology that offers a wide range of techniques and innovative concepts to the study of human behavior. The DST is focused on the study of how dynamical systems evolve in time and is specifically centered in the study of nonlinear dynamic systems.

Human beings are excellent examples of dynamic systems that behave in a nonlinear way and are constantly changing. Traditionally, the study of human behavior and psychopathology has focused almost exclusively in a unique temporal moment and the process of change has been usually conceived as organized and progressive, following a linear conception. This is far from reality since the experience has shown that sharp and sudden changes are quite frequent in human behavior. Therefore, the traditional perspective has tried to embrace the complexity of human behavior from a reductionist point of view, resulting in an excessive simplification of an enormously complex phenomenon.

The DST considers nonlinearity of human beings and offers a more appropriate approach to study the complexity of these systems. According to Thelen (2005), this new approach can dramatically change our current knowledge about psychopathology and represents a flexible and time-dependent method to get into the complexity of humans' behavior. However, this perspective is quite unknown for specialists in Psychology. For that reason, this chapter is aimed at clarifying some of its main concepts.

2.1. Introduction to nonlinear dynamic systems

Linear and nonlinear dynamic systems have different features that make them behave distinctly, and it is important to understand the main differences between them (see Bornas, 2016). First, linear systems have a quality called superposition. This means that if a series of inputs generate a certain output, the sum of the inputs will produce the same output. Nonlinear systems do not accomplish that feature since the inputs do interact with each other when "inside" the system and it can result in a very different output. Second, linear systems usually respond to the input proportionally. Thus, if we double the size of the input, the size of the output will also be doubled. Regarding nonlinear systems, big inputs can cause small outputs and small inputs can cause big outputs, so the response of a nonlinear system does not depend on the size of the stimulus. Finally, nonlinear dynamic systems are characterized by seemingly random behavior, but their behavior is actually deterministic. Contrary to random systems, deterministic ones are controlled by rules, and therefore it might be possible to predict their behavior (at least up to a point) by discovering the general patterns that they follow. In time series of deterministic systems, the previous values influence the posterior values.

2.2. Physiology and complexity

The DST has had a deep impact on the study of the physiological domain. The human organism is constituted by several control mechanisms that are continuously interacting with each other, maintaining the system within a range of specific parameters. There are so many interrelated causes and effects of physiological processes that it is impossible to take into account all the variables that influence them. These regulation processes are not linear, i.e. based on the typical stimuli – response scheme, but take into account a myriad of intermediate processes that are internal (of the own individual) and external. The output of these processes (assessed through several body responses such as heart rate, blood pressure, etc.) can show the complexity of the underlying systems interactions. Physiological complexity can be quantified using nonlinear measures within the DST framework.

2.2.1. Fractality and scaling

A fractal, term formally introduced by Mandelbrot (1967), is usually an object whose structure always resembles the whole set when observed at different scales, displaying self-similarity (Ary L. Goldberger, Rigney, & West, 1990). Fractals are ubiquitous in nature and typical examples would be broccoli or cauliflower. The following image can help to clarify what a fractal object is:

If we take a look at the broccoli's florets, we can see how each floret seems to be a thumbnail broccoli.

Similar to objects, temporal series of data from physiological systems can also fluctuate following a fractal structure. In that case, no specific scale is controlling the system, i.e. the system has different set points and operates at distinct time scales (scaling), showing scale-free behavior and multistability, thus increasing the complexity of the system. There is a large body of evidence that demonstrates the presence of scaling properties of many physiological systems (Goldberger & West, 1987; Goldberger, 1996; Hausdorff et al., 1996; Peng, Havlin, Stanley, & Goldberger, 1995; West, 1990). Concretely, in the nineties Goldberger (1996) proved that the heart beat fluctuations were not random, but fractal. Complex systems need to operate at multiple time scales, since only responding to a single time-scale cannot be sufficient for a better adaptation to a constant changing environment. As pointed out by Pittman-Polletta, Scheer, Butler, Shea, and Hu (2013), the fractal or self-similar patterns in physiological fluctuations are intrinsic and contain hidden information about the health of the regulatory system producing these fluctuations (p. 874). Therefore, specific changes like vagal withdrawal or sympathetic activation would occur at a real time scale in response to specific stimuli, but they would also be embedded into a complex self-similar structure of the cardiac system. Hence, it seems reasonable to not forget the multiscale global structure when investigating sympathetic or parasympathetic fluctuations.

2.2.2. Homeostatic versus allometric control

Traditionally it has been assumed that homeostasis is the main regulatory mechanism of physiological fluctuations, returning the system to its basal level and maintaining an internal balance when the systems deviate from its single set point (Cannon, 1929). Homeostatically controlled systems react to what is happening now, at the present moment, and operate by negative feedback cushioning environmental disturbances. For years, it was thought that fluctuations of physiological systems were random variability around a set point; i.e. the heart beat fluctuations as variations around a mean heart rate. Despite the wide recognition of homeostatic control, this type of regulation is not sufficient in itself to account for the high complexity presented for many systems, especially the physiological ones.

As formerly mentioned, physiological systems have different set points (not only one, as homeostasis predicts). When that happens, the system is controlled by another regulatory mechanism: the allometric control (West, 2006). This mechanism operates at different time scales (scaling), taking into account not only what happens in the present, but also what has happened in the past, proving the existence of a built-in long-term memory process involved in their functioning. Thus, allometric control would enhance the flexibility and complexity of the underlying systems by introducing a fractal character into seemingly random time series and creating multistability. Higher complexity allows the system to adapt to its constantly changing everyday life environment (Goldberger, Peng, & Lipsitz, 2002; Lipsitz, 2004).

2.2.3. Regularity and disease

Not so many years ago, it was thought that systems which behaved in a regular way were healthier than those which behaved irregularly. In fact, systems with irregular behavior were thought to be associated to diseased conditions. Nowadays, there is evidence that regularity and health are not synonyms, and that irregularity is not the result of random and unknown processes, but the product of nonlinear relationships between the variables. Even more, over the last years a growing number of studies have proven that a certain level of irregularity is healthy and necessary to achieve a better adaptation of the system to the environment (Goldberger et al., 2002; Lipsitz, 2004).

Deviations or fluctuations over time from various set points (multistability) would be inferred as the result of processes competing for control the system. In his pioneer study about the fractal nature of the cardiac response, Goldberger (1996) concluded that the regularity of the heartbeat increased the probability of developing a cardiac pathology in the future, such as myocardial infarction. After this discovery, many authors have proven that a regular, non-variable system's behavior across different time scales is usually associated with disease and aging (e.g. Goldberger et al., 2002; Sturmberg, Bennett, Picard, & Seely, 2015). Hence, variability and complexity become desirable aspects in the DST, because they provide flexibility to the system and allow the individual to evolve and adapt in a constant changeable environment. However, we must be careful and not confuse variability with randomness. Variability is a feature observed in deterministic time series. As mentioned earlier, in deterministic time series the previous values influence the posterior values. That means that some values are more likely to be displayed, depending on the previous conditions of the system. In contrast, in a random series there is the same probability for every value to appear.

Even though variability has been considered an adaptive characteristic, an excessive amount of variability can also be detrimental. For instance, individuals with panic disorder have shown excessive irregularity and complexity in their respiratory patterns (Caldirola, Bellodi, Caumo, Migliarese, & Perna, 2004). Over the last years, a novel concept has emerged from theorists of the DST: the optimum variability (Schuldberg, 2015). This concept is defined as the most desirable level of variability in the direction the system moves over time. According to Guastello (2015), the complex systems' values of variability are mid-range, and both too much and too little complexity can be considered detrimental to optimal functionality (implicating little stability or organizational constraint respectively). Therefore, the degree of variability shown by a system would be optimal when it maximizes benefits and reduces costs simultaneously.

3. Application of the dynamic systems theory to the study of vulnerability factors for internalizing disorders

As a summary, applications of the DST might help to gain a better understanding of the complexity of human beings. Specifically, the present doctoral thesis aims to shed some light about vulnerability factors related to the etiology of IDs, following a DST framework. It is worth remembering that a better knowledge of the vulnerability factors implied in the genesis and maintenance of IDs is crucial in preventing the appearance of these disorders. An effective prevention would drastically reduce the impairment and suffering of the individuals and their relatives, as well as the economic cost of these conditions for the public health system.

The current doctoral thesis is centered in two main aspects following the DST: the cardiac complexity and the affective fluctuations of early adolescents.

3.1. Cardiac complexity

Interest in HRV and cardiac complexity (CC) has grown in the last 30 years. Goldberger (1996) provided a rationale considering the DST (and derived concepts) for the study of physiological systems dynamics and stated that classic homeostatic models were unable to explain complex fluctuations in heartbeat. From a clinical perspective, (Captur, Karperien, Hughes, Francis, & Moon, 2017) have also stressed the need to consider the cardiovascular system as a complex system, and specifically the utility of nonlinear cardiac measures in the study of its behavior.

In this vein, complexity has been proposed as a hallmark of health (Costa, Goldberger, & Peng, 2005; Goldberger et al., 2002). Complexity of a physiological system emerges from structural units and regulatory feedback loops that indicate the continuous interplay of multiple dynamic processes at different physiological levels of organization. These dynamics operate at different time and spatial scales increasing the flexibility of the system and enabling better adjustment to demands. Specifically, CC refers to the level of sophistication of the cardiac system dynamics. Higher levels of CC allow the cardiac system to successfully adapt to an everyday life environment in constant change (Goldberger et al., 2002) and therefore, is related to the level of health and flexibility displayed by the system. In fact, it is known that CC decreases with age (see Pikkujämsä et al., 1999) and disease (De la Torre-Luque, Bornas, Balle, & Fiol-Veny, 2016; Goldberger et al., 2002). It has been also stated that under certain conditions CC decreases temporarily (e.g. stress, see Schubert et al., 2009).

Complexity is a broad concept and there are several estimators for its measurement. Each of them reflects complexity from different approaches, focusing on distinct properties such as dimensionality, regularity or predictability. Scaling and entropy are important properties to take into account when determining CC. Almost all measures of scaling and entropy consist of calculations performed on interbeat intervals time series extracted from ECG recordings.

As previously said, scaling properties suggest that the heart regulatory system operates at different time scales (Goldberger et al., 2002; West, 2006). A widely used method to quantify the scaling or fractal structure of a time series is the *detrended fluctuation analysis* (DFA; Peng et al., 1995). DFA quantifies the scaling exponent α, an index that estimates temporal correlations of a power-law form embedded in interbeat interval (IBI) time series. These long-range correlations mean that the heartbeat requires some regulatory mechanisms more complex than homeostatic ones. Another method to quantify scaling from a time series is the allometric aggregation, a relatively new method developed by West (2006). The scaling exponent *h* is obtained by examining the invariance of the relationship between the mean and the standard deviation of a data series as the data points are iteratively aggregated, thus decreasing the resolution (scale) of the series. This method is comparable to more sophisticated methods, such as DFA, although it requires less data (West & Brown, 2005), p. 231). Finally, another method created to calculate scaling is Higuchi's fractal dimension (HFD; Higuchi, 1988). This algorithm is a nonlinear measure in the time domain and stands out for its speed, accuracy and cost of applying in the study of physiological complexity (see Kesić & Spasić, 2016 for a review).

In addition to scaling properties, complex healthy systems are generally less predictable and more irregular than simple or diseased systems (De la Torre-Luque et al., 2016; Goldberger et al., 2002). Entropy quantifies the predictability and irregularity of a time series by the rate of new information that the system generates as it evolves (Pincus & Goldberger, 1994; Pincus, 1991). According to Bravi, Longtin, and Seely (2011) entropy is one of the most promising measures in the informational domain to study the complexity of a system. Opposite to linear HRV measures, which consider irrelevant the order of presentation of the interbeat intervals, time order is crucial for entropy measures because they refer to probabilities that specific patterns of successive values appear again in the time series. Thus, whereas variability only refers to dispersion, entropy refers to irregularity and predictability. The time order of the interbeat intervals is important when quantifying CC since it emerges from the dynamical nature of the heart regulation system. Sample entropy (Richman & Moorman, 2000) and multiscale entropy (M. Costa, Goldberger, & Peng, 2002) are widely used methods for quantifying entropy.

3.1.1. Cardiac complexity and internalizing problems

Scientists have recently stressed the utility of nonlinear measures in understanding the relationship between physiological and psychological variables (De la Torre-Luque et al., 2016; Young & Benton, 2015). Traditionally, this type of studies had been focused

on the sole use of linear measures. However, in the past few decades, the study of the CC has provided relevant knowledge for a better comprehension of the relationship between cardiovascular dynamics and IDs. Recently, a meta-analytical review conducted by De la Torre-Luque et al. (2016) concluded that the cardiovascular system of healthy adults show higher levels of CC than the system from individuals who suffer from an ID, thus lending support to the complexity loss theory (Goldberger et al., 2002) and considering CC as a biomarker for this type of disorders.

Literature regarding CC and internalizing problems in adolescents is still scarce. Over the last years, our research group has focused on studying cardiovascular regulation in adolescents with and without risk for anxiety disorders and has found some relevant results. For instance, Balle et al. (2013) reported lower levels of cardiac entropy across different experimental conditions for adolescents at risk for anxiety disorders than for their healthy counterparts. Bornas et al. (2015) calculated fractal dimension and entropy on long cardiac recordings in ecological conditions and reported that both measures were significantly lower in adolescents with high anxiety symptoms than in adolescents with low anxiety symptoms. De la Torre-Luque, Fiol-Veny, Bornas, Balle, and Llabres (2017) found heart rate entropy under stressful conditions useful in distinguishing adolescents with increasing trajectories of anxiety symptom from those with non-increasing trajectories. In another study, Fiskum et al. (2018) stated that sample entropy significantly predicted internalizing psychopathology and negative effects in children with internalizing problems and healthy controls. In conclusion, notwithstanding the lack of literature in children and adolescents, the available data seem to point to a lower CC in adolescents at risk for IDs.

3.1.2. Cardiac complexity and emotion regulation

In parallel to the integrative model proposed by Beauchaine and Thayer (2015), there is another emotion regulation model framed within the DST (Thayer, Ahs, Fredrikson, Sollers III, & Wager, 2012; Thayer & Lane, 2000). Briefly, the model of neurovisceral integration in ER (Thayer et al., 2012; Thayer & Lane, 2000, 2009) conceives HRV as the result of the interplay between sympathetic and parasympathetic influences on the heart rate. In turn, these influences are controlled by a network of brain structures or subsystems implied in self-regulation processes. Thereby, subcortical structures underlying the defensive behavior would be under the inhibitory control of prefrontal areas of the brain. This inhibitory neural circuits would be important for goal-oriented behavior and for flexible responses to situational demands. These authors place reduced flexibility of cardiac vagal tone, measured as HF-HRV, as a general vulnerability to psychopathology.

In line with this model, nonlinear measures would be more able than traditional linear models to capture the dynamical nature of the cardiovascular subsystem and the feedback and feedforward mechanisms that influence its regulation. This information would help to gain a more representative understanding of the relationship between cardiac regulation and ER. In accordance with this hypothesis, Fiskum et al. (2017)

already concluded that sample entropy could be a potential biomarker of dysregulation in the underlying neurovisceral processes for ER.

As stated in the first chapter, there are studies relating specific ER strategies or general ER styles with cardiac adjustment or maladjustment in front of stress in adolescent and adults (e. g. Aldao et al., 2014; Berna et al., 2014; Ottaviani et al., 2016), but their results are still inconclusive. Additionally, according to Burke, Davis, Otte, and Mohr (2005), psychosocial factors rarely predict vagal recovery after laboratory-based stressors. However, we must notice that all these studies have used linear measures. Perhaps, psychological factors such as ER strategies, are weakly associated with linear features, but strongly associated with nonlinear features of the cardiac output.

3.1.3. Cardiac complexity and sex

Little is known about sex differences in CC since most of the studies of cardiac regulation have focused on linear measures of HRV only. However, Bobkowski et al. (2017) did not find sex differences in HRV by calculating Poincaré plots-related indexes (a nonlinear measure) in 24 h recordings from 100 children and adolescents. As far as we know, no studies have used nonlinear measures of complexity when studying adolescent sex differences in cardiac response under ecological conditions on one hand, and under laboratory-elicited stress on the other. Therefore, whether adolescent males and females show differences in CC during everyday life or under the impact of acute stress remains unknown to a large extent. Finally, none of the commented-above studies about CC differences between adolescents at risk for anxiety disorders and healthy counterparts performed sex-related analyses. To gain some understanding of the presence of these differences may help to detect whether adolescent males or females are more physiologically vulnerable to develop IDs, and if this is the case, design prevention programs oriented to enhance complexity of the cardiovascular system of the vulnerable group.

3.2. Affective fluctuations

First of all, it is essential to clarify that affect and emotion are not the same concept, even though they have been used in an undifferentiated way. In general, affect is referred to a wider category that includes emotion and emotional state. An emotional state can last hours or even days, with low or moderate levels of intensity. On the other side, emotions are usually more ephemeral and discrete, generating an intense influence on the individual and more autonomic responses (Power & Dalgleish, 1997). Furthermore, emotions usually have a clear start and ending whereas the emotional states evolve gradually, without clear limits in its beginning and ending (Larsen, 2000).

Bearing this in mind, we are going to focus on affective fluctuations. Although affect stability was traditionally considered a central component of health and well-being (Costa & McCrae, 1980; Eysenck, 1967), recent research suggests that resilience relies on the ability to flexibly switch and adapt our emotional responses to environmental demands (e.g., Waugh, Thompson, & Gotlib, 2011). As a result, concepts such as ER flexibility or psychological flexibility have emerged and have been related to different psychological disorders, such as depression or anxiety (Aldao, Sheppes, & Gross, 2015; Kashdan, 2010; Koval, Kuppens, Allen, & Sheeber, 2012).

Typically, research in affect has focused on states, using data assessed on specific moments and linear statistical methods, to find out if treatments or variable manipulations provoke any effect on the variable outcomes. However, these measures do not capture complete real time evolution, being reductive in the process of change's explanation. Analyzing the variability of affective time series and considering their nonlinear properties, through techniques derived from the DST, provides more information of the system's behavior than the simple average of the data (Kashdan, 2010; Kuppens, Oravecz, & Tuerlinckx, 2010). In our opinion, "the necessity for a fractal view of physiology that explicitly takes into account the complexity of living matter and its dynamics" (p. 1) emphasized by West (2010) should be adopted for studying affect changes as well, since it could help to discover hidden patterns across multiple time scales and reveal how emotions are regulated. However, scaling properties in psychological fluctuations have received scientific attention only recently. Previous research has demonstrated the fractal structure of processes such as self-esteem (Delignières, Fortes, & Ninot, 2004) or work motivation (Navarro, Curioso, Gomes, Arrieta, & Cortes, 2013) in healthy adults. Regarding affective fluctuations, Gottschalk, Bauer, and Whybrow (1995) found more rigid and organized daily mood fluctuations in adults with a bipolar disorder than in healthy controls. Further, adult psychiatric patients showed higher mood variability but less complexity than healthy controls (Woyshville, Lackamp, Eisengart, & Gilliland, 1999).

Scaling behavior is adaptive because it helps to prevent excessive "mode-locking," interpreted here as a rigid association between a stimulus and an affective response. In this situation, it seems plausible that not only homeostatic, but also allometric control mechanisms are in charge of regulating these fluctuations. Thus, the system would respond to each disturbance at the present moment, but also taking into account previous fluctuations and responding with self-similar patterns. This would imply the existence of a built-in long-time memory process that helps the system to behave considering different time scales and showing multistability. The presence of scaling in affective fluctuations is in accordance with the socioemotional flexibility model developed by Hollenstein, Lichtwarck-Aschoff, and Potworowski (2013) within the DST framework. This model considers that flexible human systems show variability over time across different timescales. Concretely, they proposed the existence of three main scales that interact with each other: micro, meso and macro. The microscale would reflect the real-time scale, e.g. fluctuations in affect within a specific situation or cardiac variability in front of a stressful situation. The mesoscale would perceive the flexibility or rigidity across contexts, thus focusing on changes in ER, internalizing symptomatology, etc. The macroscale would consider the variability that occurs across longer periods of time (i.e. months or years), reflecting flexibility due to development. In this scale, flexibility of stable constructs

would be considered, such as temperament or personality. Additionally, this model assumes the dynamic interaction between the variability patterns across timescales. For instance, interactions between temperament (macro) and internalizing symptoms (meso), or between cardiac variability when confronting stress (micro) and emotion regulation (meso).

As far as we know, only one study has focused on the scaling properties of affective fluctuations in healthy adults (Bornas et al., 2015). Thirty-two undergraduates reported their mood and anxiety on a daily basis over a 50-day period. Scaling exponents, calculated through the allometric aggregation method (West, 2006), confirmed that participants' mood and anxiety fluctuations showed scaling behavior. This may seem surprising because good and bad things are supposed to happen randomly in everyday life (at a real-time scale), so we would expect our mood or anxiety level to change randomly too. This apparent paradox can be resolved by taking into account not just real time but other longer time scales. Positive and negative events usually take place in minutes or hours, but their occurrence is embedded in one specific day that is embedded in a week, which is, in turn, part of a longer period of time and so on. Therefore, the system is multistable, i.e. it behaves at different time scales and adjusts itself around different set points. These authors also reported negative relationship between anxiety scaling exponents and positive ER strategies.

As previously stated, adolescence is a highly changeable period of development (Hollenstein & Lougheed, 2013) accompanied by an increase in perception of stress and daily hassles (Larson & Ham, 1993; Seidman et al., 1994). Therefore, it is not surprising that adolescents' affect often seems to be a roller coaster, characterized by rapid emotional shifts. However, in accordance with the little evidence obtained with adults, adolescents' affective fluctuations might not be as random as they look. To the best of our knowledge, there is no evidence yet of the multi-stability (i.e. the scale-free behavior) of mood or anxiety fluctuations in adolescents.

4. Objectives and hypotheses

4.1. General objective

Over the course of the background and the general framework, a number of shortcomings and gaps have been flagged in the study of the etiology and related vulnerability factors for IDs in adolescents. Additionally, a new perspective that is reshaping our understanding of psychological and physiological processes has been introduced. In general terms, this doctoral thesis aimed at shedding some light into diverse aspects of the cardiovascular and affective system that are related with internalizing problems, using the DST as a main framework. For that purpose, samples of healthy adolescents were used for all the studies, since adolescence is a critical developmental stage for the development of IDs. Furthermore, as many of the research on this subject has been carried out under resting laboratory conditions, adolescents were mostly assessed in ecological or in stressful laboratory conditions. As a result of exposing adolescents to different circumstances, it was expected to obtain better representation of cardiovascular and affective real-life dynamics.

4.2. Specific objectives and hypotheses

The current thesis has resulted in 5 publications on scientific journals with specific objectives and hypotheses that will be further described hereafter.

- **Publication 1.** The objectives of this study were: a) to test whether daily mood, anxiety and worry fluctuations in a sample of healthy early adolescents (N = 25) were under allometric control and b) to explore their relationship with anxiety symptomatology and temperament factors. The hypothesis for the first aim was that all the scaling exponents would confirm that affective fluctuations of adolescents are under allometric control and show multistability. As to the second aim, it was expected that mood, anxiety and worry scaling exponents would correlate positively with each other, sharing a pattern of fractality. It was also predicted that anxiety and worry scaling exponents would be positively associated with negative affectivity and anxiety symptomatology, but negatively associated with effortful control. No associations were estimated for mood scaling exponents.

- **Publication 2.** This study aimed at elucidating whether, under ecological conditions, a sample of early adolescents (N = 95) manifested differences in HRV and CC, depending on their sex (males vs females) and level of anxiety (high- or low-anxiety symptomatology). Based on previous research, higher mean heart rate, lower HRV and lower CC were expected for the high-anxious group, as well as for females.

- **Publication 3.** The main objective was to detect whether, under ecological conditions, a sample of early adolescents (N = 166) showed sex differences in their HRV and CC. It was also intended to explore whether sex and measures of HRV and CC, as well as their interaction, predicted levels of internalizing symptoms. Similar to publication 2, it was hypothesized that females would show lower levels of HRV and CC.

- **Publication 4.** The first aim was to examine the relationships between negative and positive ER styles and (a) steady-state cardiac regulation (hear rate, HRV and heart rate entropy) at rest and under stress, and (b) the cardiac reactivity to and recovery from a stressful condition (i.e. the changes from one state to another), in a sample of early adolescents (N = 89). The hypotheses were that a negative ER style would interfere with heart rate recovery after the removal of the stressful condition, and would significantly predict heart rate, HRV and heart rate entropy, as well as changes in these variables, even after controlling for anxiety symptomatology. A second aim was to compare two groups with different ER styles under stress induction. Differences in HRV and heart rate entropy were predicted between adolescents with a highly negative ER style (adolescents who are prone to use negative ER strategies) and their low negative ER style counterparts (adolescents who are less prone to use negative ER strategies). Due to the known associations between ER and anxiety psychopathology, those differences were estimated to be smaller after controlling for anxiety symptomatology scores. Adolescents with a more negative ER style were expected to show less HRV and heart rate entropy than adolescents with a less negative ER style.

- **Publication 5.** The first aim was to analyze the cardiac pattern of healthy adolescents (N = 92) across the conditions of a stress induction protocol. It was expected for linear cardiac measures to follow the normative pattern in response to stress (i.e. heart rate increases and HRV decreases in response to stress, as well as heart rate decreases and HRV increases during the recovery from stress). Based on theoretical assumptions, a pattern similar to the normative heart rate pattern was predicted for scaling exponents, whereas entropy and fractal dimension were expected to decrease in front of stress and increase thereafter, similarly to HRV linear measures. The second objective focused on detecting sex differences in HRV and CC across the different stages of the stressful protocol. The main hypotheses were that females, in comparison to males, would show (a) higher responsiveness of the sympathetic nervous system during the confrontation and the recovery conditions (i.e. higher HR and scaling exponents), (b) greater reduction of the parasympathetic nervous system influence during stress and less recovery of the parasympathetic system from stress (i.e. lower RMSSD), and (c) lower cardiac entropy and fractal dimension during the exposure and the recovery conditions. As a last aim, the existence of sex differences was analyzed in the self-perceived performance-anxiety in response to the stressful tasks. In line with previous evidence, higher levels of performance anxiety for females were expected in both stressful tasks (public speech and math).

II. Publications

1. Fiol-Veny, A., De la Torre-Luque, A., Balle, M., & Bornas, X. (2017). Allometric control of affective fluctuations in early adolescents: their association with anxiety symptoms and temperament traits. *Nonlinear Dynamics, psychology, and Life Sciences, 21,* 255 – 266. http://www.societyforchaostheory.org/ndpls/askFILE.cgi?vol=21&iss=03&art=01&desc=ABSTRACT

2. Fiol-Veny, A., De la Torre-Luque, A., Balle, M., & Bornas, X. (2018a). Diminished heart rate complexity in adolescent girls: a sign of vulnerability to anxiety disorders? *Anxiety, Stress & Coping, 31,* 375 – 386. https://doi.org/10.1080/10615806.2018.1475004

3. Fiol-Veny, A., De la Torre-Luque, A., Balle, M., & Bornas, X. (2018b). Altered heart rate regulation in adolescent girls and the vulnerability for internalizing disorders. *Frontiers in Physiology, 9,* 1 – 11. https://doi.org/10.3389/fphys.2018.00852

4. Fiol-Veny, A., Balle, M., De la Torre-Luque, A., & Bornas, X. (2019). Negative cognitive emotion regulation as a predictor of adolescent heart rate variability and entropy under social stress. *Anxiety, Stress & Coping, 32,* 641 – 653. https://doi.org/10.1080/10615806.2019.1641199

5. Fiol-Veny, A., Balle, M., Fiskum, C., & Bornas, X. (2019). Sex differences in adolescents' cardiac reactivity and recovery under acute stress: the importance of nonlinear measures. *Psychophysiology.* https://doi.org/10.1111/psyp.13488

III. Discussion and conclusions

This doctoral dissertation aimed at shedding some light on the vulnerability of developing an ID. A first general question was formulated: can cardiac and affective complexity indexes help to distinguish between healthy adolescents more vulnerable and less vulnerable to experience IDs? Then, a second question was raised: how are affective and cardiac complexity from healthy adolescents related to other established IDs-related vulnerability factors, such as sex, internalizing symptomatology or emotion dysregulation? For this purpose, the dynamics of cardiovascular and affective systems of healthy adolescents were studied under ecological and under laboratory stress conditions, following a rationale based on the DST. The results from the five studies carried out allowed us to answer the questions raised by this investigation.

10. General discussion

10.1. Affective complexity

In the study 1, a sample of healthy adolescents reported their daily mood, anxiety and worry levels twice a day over a period of 100 days. Almost all scaling exponents (mood, anxiety and worry) proved their fractal nature and multistability, similarly to the results found with adults (Bornas et al., 2015). That means that affect is not just controlled by homeostatic mechanisms, which are only based on what is happening at the present moment (real-time scale), but mainly by allometric mechanisms. Therefore, the affective system of healthy adolescents would have different set points and operate at distinct time scales, suggesting the presence of a built-in memory that also allows to respond to what has happened in the past. As stated in the introduction section, the fractal structure of a system's fluctuations increases its flexibility and complexity and endows the system with greater ability to adapt to contextual demands in constant change.

Regarding the relationship between affective complexity and other IDs-related vulnerability factors, the study 1 showed that worry exponents were positively correlated with effortful control, and negatively associated with negative affectivity and affiliativeness. As scaling enhances the flexibility of the underlying system, it makes sense for individuals with lower worry exponents, i.e. less flexibility, to show lower self-regulatory skills since their affect would be exclusively locked to the incoming stimuli. On the other hand, it is also reasonable that adolescents with lower worry exponents tend to display more negative emotions, as they probably have more difficulty in responding adequately to contextual demands. This interpretation would be coherent with the negative relationship found between worry exponents and affiliativeness. It seems that

adolescent with more random worry fluctuations (and poor effortful control) might need more social support than those with more complex worry fluctuations.

10.2. Cardiac complexity

The study 2 and study 3 were highly related in terms of aims, hypotheses and methodological strategy. Both studies were performed under ecological conditions as the cardiac activity of adolescents was recorded during 120 minutes while they were performing regular activities within the academic context. In the study 2, four groups of adolescents were created according to sex (female/male) and anxiety symptomatology (high/low). For the study 3, a larger sample of healthy adolescents was randomly selected, regardless their level of anxiety symptoms. The studies 4 and 5 were also related, as they both were conducted under stressful laboratory settings. The study 4 consisted of a sample of healthy adolescents that underwent a socially relevant stress induction protocol while their cardiac activity was recorded. Subsequently, the ER style of the individuals was used to select a subsample conformed by two groups (adolescents with a high negative ER style and adolescents with a low negative ER style). Finally, the study 5 consisted on recording the cardiac activity of a sample of healthy adolescents while they were exposed to a social stress induction protocol.

The question whether CC can help to distinguish between healthy adolescents more vulnerable and less vulnerable to experience IDs, was originally based on previous findings that propose linear measures of vagally-mediated HRV, such as cardiac vagal tone, as transdiagnostic biomarkers for IDs (e. g. Balzarotti et al., 2017; Beauchaine & Thayer, 2015). Under ecological conditions, linear HRV measures were useful in distinguishing adolescents with high and low anxiety symptoms (study 2), and between males and females (study 2 and 3). Both adolescent females and adolescents with higher level of anxiety symptoms showed lower cardiac vagal tone, in line with previous literature (Balle et al., 2013; Dietrich et al., 2007; Faulkner et al., 2003; Koenig et al., 2017; Silvetti et al., 2001). Since subclinical levels of anxiety and depressive symptoms, on the one hand, and female sex on the other, have been indetified as vulnerability factors towards internalizing problems (Balázs et al., 2013; Essau et al., 2018; Fergusson et al., 2005; Goldman, 2012; McLean et al., 2011; Shankman et al., 2009), these findings add support to the consideration of cardiac vagal tone as a transdiagnostic biomarker for IDs. Linear measures were not as useful in distinguishing between adolescents with functional and dysfunctional ER styles under steady stressful circumstances (study 4), but those with a higher maladaptive ER style had lower changes in HRV from baseline to stress, and from stress to recovery, showing a more rigid cardiac regulation. Besides this, values of linear HRV from females and males were not significantly different under stress either (study 5).

Focusing on CC and sex, the complexity of the heartbeat was found to be lower in females as compared to males (study 2, 3 and 5). Concretely, adolescent females showed faster decays in long-range temporal correlations (lower fractality) and higher predictability of their IBIs time series at longer time scales (lower entropy) in ecological

conditions (study 2 and 3) and under a stressful task (study 5). Thus, not only the real-time function of the parasympathetic system would be reduced in females, but also the cardiac fractal and irregularity properties. These results seem to point to a less complex organization of the cardiovascular system in females and suggest that females would be more "physiologically" vulnerable to the development of internalizing problems. In terms of ER, the study 4 showed that adolescents prone to use more negative ER strategies had more CC, i.e. a more irregular heartbeat, during the acute stress (contrary to our initial hypothesis), but at the same time lower CC from stress to recovery (in accordance with the original hypothesis). In a meta-analytic review, De la Torre-Luque et al. (2016) already reported inconsistent results from studies using entropy measures, since diseased systems that show erratic behavior may have very high entropy values. Although its meaning is not clear yet, all indicators seem to point at the importance of cardiac entropy in the study of ER and internalizing disorders (Fiskum et al., 2017, 2018). However, it is important to highlight that the interpretation of the studies under stressful settings must be done carefully. A decrease in cardiac variability and complexity during stressful events can be considered normative and a sign of adaptive self-regulation, at least within a range. Systemic complexity has been related to systemic adaptability (Lipsitz, 2004), but following the hypothesis of the optimal variability (Guastello, 2015; Schuldberg, 2015) both too much and too little complexity can be considered detrimental. Unfortunately, we do not know the optimal levels of CC in adolescents during stress yet, so we cannot conclude which group (females or males, high or low negative ER style) showed the most adaptive cardiac response.

The second question, regarding how cardiac complexity from healthy adolescents related to other established IDs-related vulnerability factors, was mostly responded by the studies 3 and 4. In general terms the prediction analyses showed that the lower the cardiac vagal tone or the CC, the higher the internalizing symptoms (study 3), similarly to other studies with adolescents under comparable conditions (Bornas et al., 2015). This fact suggests different amounts of complexity in the cardiac regulation of adolescents regarding their level of anxiety. Therefore, the lack of differences between adolescents with high and low levels of anxiety symptoms in the study 2 could be due to the small sample size. Additionally, the entropy of the IBIs time series during the social stressful task was predicted by sex and negative ER style scores (study 4). On the one hand, the sex female predicted lower heart rate entropy. On the other hand, a higher irregularity of the heart rate during the exposure condition was related to higher levels of negative ER style. Finally, the results indicated that the more the negative ER style, the lesser the changes in HRV reactivity, and in HRV and CC recovery.

A final relevant issue, not related with the two general questions but important enough to be mentioned, would be the comparison between linear and nonlinear measures in itself. Linear measures showed sex differences in the cardiac response of healthy adolescents under ecological, but not under stressful conditions. Furthermore, a dysfunctional ER style was related with cardiac entropy under stress, but not with other lineal HRV measures. Therefore, it seems that when considering stress-induced changes, the use of linear measures is insufficient and nonlinear measures can offer higher sensitivity to discriminate between adolescents with different levels of vulnerability to IDs. Nonlinear measures also provided additional information that helped to increase our knowledge of how the cardiovascular system of healthy adolescents operates under

ecological conditions. These findings add support to the necessity of using nonlinear measures when analyzing cardiovascular dynamics and their relationship with psychological vulnerability factors for internalizing problems (Captur et al., 2017; De la Torre-Luque et al., 2016; Thayer et al., 2012; Thayer & Lane, 2000, 2009; Young & Benton, 2015).

11. General conclusion and limitations

In general terms, this doctoral thesis proves that affective and cardiac fluctuations of healthy adolescents are under complex regulation processes that have memory and take into account information from different time scales, to successfully adapt to their daily life. It is also concluded that healthy adolescents more vulnerable to IDs (females, higher internalizing symptoms or emotion dysregulation strategies) seem to have lower levels of affective and cardiac complexity than adolescents less vulnerable. Specifically, CC under ecological conditions seems to be reliable in detecting adolescents with high vulnerability to internalizing problems. Although CC under stressful conditions needs to be further investigated in order to obtain a certain interpretation of their physiological meaning, it is obvious that adolescents with different levels of vulnerability have distinct levels of CC. This thesis supports the hypothesis that adolescents with higher vulnerability to IDs have lower levels of CC. Therefore, it is posited that this attenuated cardiac flexibility/complexity may constitute a physiological marker of a maladaptive pattern to confront internal and environmental challenges.

The studies included in the current doctoral dissertation have a number of limitations. First, and regarding affective fluctuations, the main limitation was the sample characteristics of the study 1. Due to the length of time and the challenging demands of the study, only 25 out of 84 participants met the requirements for being included in the analyses. Although it was confirmed that completers and non-completers did not differ in their temperamental traits, is it possible that these two samples were not homogeneous. An indicator would be that 22 of 25 participants were females, even though the proportion of males and females enrolled in the experiment was similar. Despite the implementation difficulties and the limitations, this was a very novel study and it is worth noting the relevance of the data obtained. Second, no other physiological factors were considered in the studies. A more integrative view of IDs should take into account the effect of other physiological systems that influences cardiovascular regulation, such as endocrine or digestive systems (e.g. Kreibig, 2010; J. F Thayer & Sternberg, 2006). Regarding cardiac sex differences, the cardiac recordings of females who had the menstruation were postponed for another day. However, no other stages of the menstrual cycle were controlled even though it is suggested that they affect brain areas related to cardiac regulation (Bäckström et al., 2011). Another limitation would be the intricacy of interpreting the results derived from stress-induced studies. It is not as simple as concluding that low values of an index are detrimental whereas high values are salutary. According to the optimum variability concept (Guastello, 2015; Schuldberg, 2015), the values of variability of a complex system are mid-range. However, we still do not know what these optimal values are in specific situations, such as when adolescents are facing

a stressor. Under stress conditions, there is a decrease on HRV and CC in all healthy individuals. This is reflected by the current results, but determining that a certain level of decrease is more detrimental or more optimal than another, without knowing which are the optimal levels for adolescents in specific stressful conditions is quite hazardous. Finally, the methodological design of the studies did not allow for causal inferences between cardiac and affective complexity and other vulnerability factors related with IDs.

Despite these limitations, the current doctoral thesis overcomes some of the actual shortcomings in the study of vulnerability factors for IDs. Within a new theoretical and methodological approach, it stresses the importance of adopting an integrative view of psychopathology that will be useful in detecting individuals with high vulnerability to IDs at crucial developmental stages, such as adolescence. All this information will contribute to design more targeted prevention strategies to hinder the emergence of internalizing problems.

12. Clinical implications

The findings obtained by the current thesis encourage a change of the classical perspective in clinical settings. Since anxiety and depression disorders are highly complex phenomena, it becomes necessary to adopt a dynamic and multidimensional approach towards their prevention and intervention. In this sense, the use of strategies focused on reducing specific vulnerability factors for internalizing problems is essential, especially during adolescence, a crucial stage that encompass the median age of onset for many IDs (Essau et al., 2014; Goldman, 2012; Kessler et al., 2005). An early detection of individuals with higher probabilities of developing an ID should be a priority in clinical practice. Within this thesis, reduced levels of cardiac and affective complexity in adolescents have been pointed out as important vulnerability factors for IDs. Therefore, developing strategies targeted to enhance the flexibility of these systems could be of interest in the prevention of these disorders. Taking long and continuous pretreatment measurements of cardiac and affective complexity would be useful for: a) detecting those adolescents at risk for IDs, and b) assessing if the treatment has been effective. Even though the difficulty of this task, we think that it would be possible by selecting participants from long waiting lists and using the actual mobile phones technology that allows taking continuous measurements several times a day.

Cognitive-behavioral strategies might be used for enhancing the multistability of affective fluctuations in vulnerable adolescents, increasing their flexibility when responding to contextual demands. However, not all patients benefit from highly cognitive-verbal therapies. According to Fiskum (2019), “an integration of more physiologically oriented approaches can expand the toolbox of therapists working with dysregulated patients”. Although many forms of psychotherapy have not usually included physiology-based interventions, there are strategies that already proved their usefulness in increasing HRV. For instance, HRV biofeedback is a technique focused on improving HRV, that have shown promising effects on the treatment of individuals with

internalizing problems (Goessl et al., 2017; Karavidas et al., 2007; Reiner, 2008; Vitasari, Wahab, Herawan, & Sinnadurai, 2011). In keeping with Lehrer and Gevirtz (2014), this technique is thought to stimulate brain regions involved in ER, such as prefrontal areas or the amygdala, through vagal afferent pathways (Grundy, 2002). Other programs, based on exercise training, have also proven their utility in increasing long-term HRV (Routledge, Campbell, McFetridge-Durdle, & Bacon, 2010). Although little is known about the effects of physiological-oriented interventions on CC, a recent study concluded that physical exercise may enhance long-term CC (Fazan, Brognara, Fazan Junior, Murta Junior, & Virgilio Silva, 2018). As the current thesis points to a greater physiological vulnerability in adolescent females, as well as in adolescents with emotion dysregulation problems, physiological-based interventions should be more oriented to these individuals. In the case of females, they showed greater physiological vulnerability but did not differ with males in the general level of internalizing symptoms. Hence, if we base interventions only on self-reported anxiety or depression scores, these females can go unnoticed and not receive protection against the development of IDs. What seems to make females more vulnerable to develop internalizing problems in the future is their reduced cardiovascular variability and complexity, thus the prevention efforts should be focused on enhancing of these properties.

13. Future research directions

The results obtained by this doctoral thesis should encourage further investigation in exploring the cardiac and affective complexity and their relationships with sex, internalizing symptoms and emotional dysregulation. Thus, on the basis of the findings obtained and their limitations, future research suggestions will be exposed.

First, the methodological design prevented from causal inferences between affective and cardiac complexity, and other vulnerability factors. Following a previous longitudinal study that suggested that the altered cardiac vagal tone might be a predictor of depression (Jandackova et al., 2016), it seems that this would be the temporal sequence. However, this cannot be assured yet and longitudinal studies need to be performed to warrant the causal relationship between the mentioned factors. In connection with the requirement of more longitudinal data, another point must be highlighted. This investigation has obtained several conclusions regarding adolescence, an especially important stage of development. Nevertheless, the conclusions obtained for adolescents might not be useful when considering other populations such as adults or elderly. For instance, a reduced cardiac vagal tone has been stated for adolescent females by this thesis and by other studies (e.g. Koenig et al., 2017), while adult females display greater levels of cardiac vagal control than males (see Koenig & Thayer, 2016 for a review). That seems to be contradictory with the results reported in adolescents, but studies on short-term and long-term HRV differences across age groups (Abhishekh et al., 2013; Moodithaya & Avadhany, 2012; Umetani et al., 1998) can help to disentangle this discrepancy. These findings highlight a lack of stability in cardiac features throughout the lifespan. In conclusion, longitudinal studies of these features across different maturational stages are mandatory.

Second, although everything seems to indicate that nonlinear indexes are useful in detecting individuals with different levels of vulnerability, we must not forget that the research on this ambit is relatively new and replication studies are needed to confirm the conclusions from the current thesis. Therefore, the use of nonlinear measures has to be incremented within the field of Psychology. That does not mean that the linear traditional methods must be discarded, but adapted to the phenomena that can be accounted for. Hence, a more dynamical view should be adopted in order to achieve a more complete knowledge about psychopathological problems. Furthermore, it would be interesting to investigate whether nonlinear indexes are also useful to detect therapeutic changes, as well as design and apply specific interventions centered on enhancing cardiac and affective complexity in order to test their effectiveness in preventing IDs. Related with that, another issue would be the lack of knowledge regarding the optimal levels of variability for each population under different conditions. For this purpose, the cardiovascular dynamics of massive samples of healthy individuals should be assessed under different conditions. With this information, conclusions about which individuals present dysfunctional levels of variability or complexity will be more reliable.

Finally, the current thesis has tried to compare the CC of healthy adolescents under ecological and laboratory-based stressful conditions. However, these studies were independent from each other since the sample of each study was different. Therefore, only qualitative comparisons could be made with this data. To obtain proper quantitative comparisons, future investigations should try to replicate these findings by using the same sample of adolescents under both type of conditions.

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