Psychosocial and Neurobiological Correlates of Past and Prospective Adolescent Suicidal Thoughts and Behaviors

By

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Abstract

Suicide is the second leading cause of death for youth in the United States and the rates are continuing to rise. Unfortunately, national policy efforts to combat this increase in youth deaths by suicide have made little difference. Suicidal thoughts and behaviors (STB) disproportionately affect female adolescents, and youth of color, including Latino youth. To date, there have been few longitudinal studies of adolescent STB in Latino adolescents, thus, many of the prospective risk factors for suicidality in these populations are not well understood. Additionally, there is limited research which has examined the neurobiological predictors of STB in community or clinical adolescent samples across all genders and ethnicities. Given this imminent and intensifying public health crisis, additional investigations are needed to examine and understand both proximal and distal factors related to the increase in adolescent STB. Moreover, as the US becomes more ethnically diverse, risk and protective factors which influence both the general population as well as specific ethnic minorities should be examined, including environmental, social, and biological factors which may act to either ameliorate or exacerbate rates of youth STB. This dissertation investigated: (1) the associations between psychosocial and culturally specific factors and the growth of STB from early to late adolescence; (2) the role of the autonomic nervous system (ANS) in stress activation during social exclusion and its relation to concurrent and prospective STB in late adolescence; and (3) whether pubertal timing moderates the link between parasympathetic stress activity and concurrent and subsequent STB in clinically high-risk adolescent females. In Paper 1, female sex and later generation status were associated with increasing prevalence in STB across adolescence, and family conflict and peer conflict predicted increased STB whereas greater familism predicted less STB, in Mexican-origin youth. In Paper 2, prior STB was associated with lower sympathetic activity at baseline and during social exclusion, and prospective STB was

predicted by lower basal ANS activity paired with greater ANS activation during social exclusion, in Mexican-origin youth. In paper 3, lower baseline parasympathetic activity and earlier pubertal timing were associated with prior STB, whereas girls with later pubertal timing and higher parasympathetic activity during a speech task were buffered from endorsing STB one year later. In summary, this body of research suggests that interpersonal processes, especially within the family, are critical for understanding suicidality risk in Mexican-origin adolescents. Additionally, basal autonomic activity may be a biomarker or a physiological "scar" of prior suicidality whereas certain patterns of autonomic stress activation may confer greater risk for prospective STB years in advance. Lastly, the female pubertal transition confers risk for STB and later pubertal timing may provide a protective buffer against STB for those youth who display dysregulated physiological responses to stress.

CHAPTER ONE

GENERAL INTRODUCTION

Suicide is now the second leading cause of death among youth aged 10- to 19-years-old in the U.S. and rates have nearly doubled in the last decade (Hoffman et al., 2020). From 2007 to 2015, visits to emergency departments for suicidal thoughts and behaviors (STB; defined as having thoughts about suicide or making plans or attempts to harm oneself with the intention of dying) sharply increased among youth aged 5- to 18-years-old (Burstein et al., 2019). In a nationally representative survey of high school students taken in the first half of 2021, during the COVID-19 pandemic, nearly 20% of adolescents had seriously considered suicide at least once and 9% had made serious attempts (Jones et al., 2022). Other previous cohort studies have revealed similar findings, demonstrating that increases in suicidality appear to be prevalent in early adolescence (Carbone et al., 2018) and epidemiological data suggest that the most severe increase in the incidence of STB occurs between 12 and 17 years of age (Nock et al. 2013). This evidence implies that adolescence represents a uniquely vulnerable window for adolescent psychopathology and that suicidality among youth is on the rise with no indication of waning.

The developmental psychopathology perspective for understanding the emergence of STB emphasizes patterns of adaptation and maladaptation, and how transactions between early adaptation, maturation, and environmental stressors influence the cascade of development, leading to both typical and atypical outcomes (Cicchetti, 1990; Rutter & Sroufe, 2000; Sroufe & Rutter, 1984). Psychopathology can be understood as a convergence of both biological and psychological vulnerabilities that lead to a weakened capacity to negotiate typical milestones (Crowell et al., 2005), especially within the context of adversity or threat.

Adolescence represents a unique period of vulnerability, considering the simultaneous changing of multiple physiological systems, and the reorganization of the social network and

social roles (Miller & Prinstein, 2019). There is significant overlap in the biological vulnerabilities and psychosocial risk factors related to STB (Crowell et al., 2014). Additionally, suicide-related behaviors are multi-determined phenomena, involving both distal factors (e.g., family dynamics, relationships with peers) and proximal factors (e.g., individual physiological stress responses, puberty). Within this framework, suicide represents the endpoint of a complex set of developmental pathways (Derbridge & Beauchaine, 2014). Indeed, this complexity is also what makes STB so empirically challenging to accurately predict in adolescents. However, there are particular risk factors which have been documented in the literature that are reliably associated with a greater vulnerability for engaging in STB during the adolescent years. Given that many correlates of STB are transdiagnostic (i.e., also pertaining to depression, internalizing symptoms), there must be greater scientific investment in studying multiple contributing factors simultaneously and over time. Therefore, using a multivariate framework to research adolescent suicidality is crucial for informing and advancing individualized treatment and early interventions, and will be the focus of this dissertation. Below, I briefly discuss how race and ethnicity, biological sex, interpersonal conflict, puberty, and the autonomic nervous system (ANS) are associated with adolescent STB.

Race and Ethnicity

Decades of research have shown that race and ethnicity are primary predictors of mental health outcomes, including STB (Brener et al., 1999; Morrison & Downey, 2000). Latino youth born in the US, compared to those born out of the country, are twice as likely to have made a suicide attempt (Fortuna et al., 2007) and second-generation Latinos are almost 3 times more likely to attempt suicide than foreign-born Latinos (Peña et al., 2008). Although Latinos are less likely than non-Latino Whites to complete suicide, they are more likely to engage in ideation and

attempts during their high school years (McKenzie et al., 2003). Ethnic discrimination and the "immigrant paradox" have both been named in discussions of the sources of mental health disparities in the U.S. The deleterious impact of perceived discrimination on mental health is well established (Araújo & Borrell, 2006; Trent et al., 2019; Vines et al., 2017) as it is robustly associated with depression and internalizing problems in Latino youth (Sirin et al., 2015; Umaña-Taylor & Updegraff, 2007; Zeiders et al., 2013), which themselves denote increased risk for suicidality. Additionally, numerous studies have documented a link between later generational status and poorer mental health outcomes in both Latino youth (García Coll & Marks, 2012) and adults (Alegría et al., 2008; Grant et al., 2004), suggesting the immigrant paradox is empirically supported and warrants additional study.

Biological Sex

Engaging in suicidal ideation and making attempts are more prevalent among adolescent girls of all ethnic groups, compared to adolescent boys (Kann et al., 2014, 2018; Rich et al., 1992; Yard et al., 2021). However, rates of completed suicides follow an opposite pattern, largely because adolescent males typically use more lethal means when attempting suicide (Grunbaum et al., 2004; Miranda-Mendizabal et al., 2019). A recent national survey of adolescent behaviors and experiences reported that females, compared to males, were nearly twice as likely to consider attempting suicide and more than twice as likely to actually attempt suicide (Jones et al., 2022). The sex differences in adolescent STB are well established but the exact mechanisms driving this disparity are still largely unknown.

Interpersonal Conflict

Adolescents who are faced with multiple stressors, especially those that are interpersonal in nature, such as parent-child conflict and peer rejection, also may be more vulnerable to

suicidality (Lewinsohn et al., 1995; Stewart et al., 2019; Wilburn & Smith, 2005;). Contemporary research has shown that social risk factors, like concurrent interpersonal stressors, may catalyze suicidal behavior for an adolescent who is already at high-risk due to prior suicidality or comorbid psychopathology (Cheek at al., 2020). There is an abundance of literature documenting the association between family conflict and adolescent suicidality, including completed suicides (Asarnow & Carlson, 1988; Brent et al., 1994; Carballo et al., 2019; Fergusson & Lynskey, 1995). Prinstein et al. (2000) reported a prospective relation between adolescents' earlier reports of overall family dysfunction and their later increased suicidal ideation. In addition, the quality of peer relationships is an important predictor of adolescent suicidality (Grudnikoff et al., 2015; Prinstein et al., 2000). Interpersonal stressors, such as being alienated by peers or being bullied, are commonly reported by youth who also engage in STB (Cheek et al., 2020; Juvonen & Graham, 2014; King & Merchant, 2008).

Autonomic Nervous System (ANS) Activity

Although there are several biological systems involved in the body's acute stress responses, the autonomic nervous system (ANS) has been implicated in several recent studies linking adolescent STB to physiological arousal and regulation (Crowell et al., 2005; Giletta et al., 2017; James et al., 2016; Kaufman et al., 2018; Wieglus et al., 2017; Yang et al., 2019). Both the sympathetic and parasympathetic branches play vital roles in regulating the body's physiological responses to safety and threat (Hastings & Kahle, 2019), and research suggests that adolescents who fail to produce adaptive and adequate physiological responses to acute stress may also be at risk of STB (Miller & Prinstein, 2019). Given the current findings, it is suggested that adolescents with and without histories of suicidality will evince differential physiological profiles, as will those youth who subsequently engage in STB.

Puberty

The onset of puberty catalyzes a neurobiological process that influences the maturation of the neural circuitry that guides behavioral and affective self-regulation (Ho et al., 2022), two facets related to adolescent STB (Hatkevich et al., 2019). The pubertal transition encompasses an array of psychological and biological changes which shape the trajectory of adolescence (Gunnar et al., 2009; Stroud et al., 2009). Early pubertal timing, or when youth enter puberty earlier compared to their same-aged peers, can influence this developmental course and has been associated with negative psychological outcomes in girls (Mendle et al., 2007), including heightened risk for suicidality (Wichstrøm, 2000). Puberty represents a period of dynamic change which can increase vulnerability for adolescent mental health problems, but also represents an optimal period for study and intervention.

The Current Studies

Despite the evidence that adolescent STB is on the rise, there remains a paucity of research that captures multiple risk factors simultaneously and longitudinally, especially in ethnically diverse samples. To cultivate a deeper understanding of the emergence and developmental course of youth and adolescent STB, prospective assessments are necessary to capture the onset of STB, how STB prevalence changes over time, and which factors are associated with this trajectory. There have been multiple calls for more comprehensive investigations of the biological and psychosocial drivers of adolescent suicidality, especially those associated with prospective engagement in STB (Cha et al., 2018; Miller & Prinstein, 2019).

Utilizing a biopsychosocial framework, this dissertation was designed to test multiple potential contributors to the emergence and development of STB in adolescence in both community and clinical samples. Study 1 was designed to examine how psychosocial factors are

related to the onset and growth of STB in a sample of Mexican-origin youth from early to late adolescence. Study 2 was designed to test whether basal and stress-responsive sympathetic and parasympathetic activity were related to lifetime history of and prospective risk for STB in Mexican-origin adolescents at risk for depression. Finally, Study 3 assessed whether basal and stress-responsive parasympathetic activity and pubertal timing were associated with prior and subsequent suicidality across the pubertal transition in a sample of clinically high-risk adolescent females.

This program of work presents research that is longitudinal in design and captures adolescent STB across development (Study 1), into early adulthood (Study 2), and over the pubertal transition (Study 3). The first study has been published in *Clinical Psychological Science* (Gonzalves et al., 2022). The adolescents included in the studies were ethnically and socioeconomically diverse, and these investigations aimed to identify how risk for STB in distinct groups (e.g., Mexican-origin adolescents, high-risk girls) was associated with various psychosocial stressors (Study 1) and individual neurobiology (Studies 2, 3). Given that very few papers have closely examined the direct relations between environmental risk and protective factors, autonomic activity, pubertal timing, and subsequent suicidality, this dissertation makes novel contributions to the literature. Furthermore, each study offers a window into different periods of adolescent development and psychopathology, culminating to build on past research (Crowell et al., 2005; Giletta et al., 2017; Yang et al., 2019) to offer new perspectives.

CHAPTER TWO

STUDY 1: PSYCHOSOCIAL PREDICTORS OF SUICIDAL THOUGHTS AND BEHAVIORS IN MEXICAN-ORIGIN YOUTH: AN 8-YEAR COHORT STUDY

Background

Suicide is the second leading cause of death among all youth aged 10 to 19 years in the United States (U.S.; CDC, 2017), with rates nearly doubling in the last decade (Hoffman et al., 2020). This is especially evident for Latino youth in general (Khan et al., 2018; Miron et al., 2019; Twenge et al., 2019), and particularly Latina youth, who have higher rates of suicidal thoughts and behaviors (STB) than youth of most other ethnic and racial communities (Kann et al., 2014; Price & Khubchandani, 2017; Villarreal-Otálora et al., 2019; Zayas et al., 2005). Despite increasing rates of STB in Latino adolescents, factors that may be driving this trend remain uncertain, because most prior research has utilized cross-sectional or short-term longitudinal studies and single-predictor analyses. In California, Latino youth constitute the majority of children aged 0 to 17 years (California Department of Finance, 2020), with the large majority identifying Mexico as their family's country of origin (i.e., Mexican-origin; Public Policy Institute of California, 2019). Therefore, identifying factors that contribute to the development of STB across adolescence in Mexican-origin youth is essential to inform the design of appropriate interventions with this rapidly growing and high-risk population (Ford-Paz et al., 2015; Standley, 2020).

To help mitigate the rising rate of adolescent suicidality in the U.S., developmental scientists focused on suicide have called for research to (1) expand how STB is defined and conceptualized; (2) focus on individual and malleable mechanisms; (3) investigate developmental trajectories of risk factors related to STB; and (4) make greater efforts to account

for diverse populations (Cha et al., 2018). Many risk factors for suicidality among Latino youth are similar to those identified for adolescents of other ethnicities (e.g., identifying as female, interpersonal conflict; Eaton et al., 2006; Kuhlberg et al., 2010), but culture-specific predictors have also been identified such as ethnic discrimination (Cheref et al., 2019; Hwang & Goto, 2008), generation status (Peña et al., 2008; Pottie et al., 2015), and less endorsement of traditional cultural values (Kuhlberg et al., 2010; Peña et al., 2011). In this study, we examined ethnic discrimination, generation status, and familism as factors that may be particularly relevant for adolescent suicidality within Latino communities, as well as family conflict, peer conflict, and sex as factors shown to be associated with adolescent suicidality across communities. Although some past research has studied various subsets of these variables simultaneously (Kuhlberg et al., 2010; Peña et al., 2011), none to our knowledge have modeled each of these risk and protective factors in a single model. Further, we used a longitudinal design spanning ages 10 to 17 years to examine whether there were specific ages at which these factors contributed to risk for STB across adolescence in Mexican-origin youth.

Predictors of STB for Latino Adolescents

Adolescence is recognized as a period of rapid social and biological changes which cumulatively contribute both to opportunity for growth (NASEM, 2019) and greater risk for psychopathology (Prinstein & Miller, 2019). To understand youth suicidality in Latino communities specifically, researchers must consider the family sociocultural environment in which these developmental changes unfold (Zayas et al. 2005). Indeed, a culturally informed developmental perspective in the examination of STB in Latino youth necessarily approaches its examination of other potentially contributing factors within the context of cultural factors (Duarté-Vélez & Bernal, 2010).

Zayas and colleagues (2005) proposed a conceptual model of Latina STB highlighting the significance of examining distal environmental factors, including both culturally specific (e.g., values) and non-specific factors (e.g., family functioning), as establishing the context of vulnerability within which proximal antecedent factors (e.g., interpersonal crises) trigger STB. Within this framework, our examination of ethnic discrimination, generation status, and familism reflect such culturally specific distal factors, whereas sex, family conflict and peer conflict constitute distal factors affecting many communities. These factors may foster either risk for or resilience against STB, but importantly, in this sample and community, both kinds of distal factors will have been experienced by Mexican-origin youth who simultaneously stand outside the dominant culture yet must exist in that society, which is often hostile to those who are perceived and categorized as immigrants or minority members. Hence, consistent with intersectionality frameworks (Crenshaw, 2017), past studies of STB in majority culture youth (i.e., European-American Whites) cannot be assumed to inform the unique and distinct ways in which culture, sex and interpersonal relationships forge contexts of risk and resilience that are experienced by Mexican-origin or other Latino youth (Zayas et al., 2005).

Ethnic Discrimination

Ethnic discrimination encompasses direct and systemic treatment of people based on their perceived non-majority social classification that disadvantages them and defines them as inferior to or different than members of the majority group (Blank et al., 2004; Jones, 2000). Nearly 40% of Latino respondents living in the U.S. report experiencing direct ethnic or racial discrimination (e.g., being told to return to their home country, being criticized for speaking Spanish; Lopez et al., 2018). The deleterious impact of perceived discrimination on mental health is well established (Araújo & Borrell, 2006; Arora & Wheeler, 2018; Stein et al., 2019; Trent et al.,

2019; Vines et al., 2017). Latino youth who experience more ethnic discrimination report more STB (Cervantes et al., 2014; Cheref et al., 2019; Gomez et al., 2011; Hwang & Goto, 2008), yet documented associations have tended to be of small to medium magnitude.

Given that adolescents spend more waking hours per day in peer and school contexts compared to other venues (Vernon, 2005), and the importance of peer group relationships for adolescent identity development and well-being (La Greca & Harrison, 2005; Ragelienė, 2016), experiencing ethnic discrimination from peers and teachers may be particularly pernicious for Latino youth (Tormala et al., 2015). A retrospective study of Latino middle- and high-schoolers found that ethnic-based bullying was related to increased suicidal ideation for depressed youth (Cardoso et al., 2018). Hence, in this prospective investigation we focused on Mexican-origin adolescents' experiences of ethnic discrimination within school settings.

Generation Status and Acculturation

Many Mexican-origin adolescents in the U.S. must navigate the dominant culture into which the current or prior generations of their family have immigrated, and generation status is a powerful predictor of psychopathology (Peña et al., 2008; Pottie et al., 2015). The "immigrant paradox" holds that those U.S. residents with foreign nativity – immigrants – are relatively protected against psychopathology than are subsequent U.S.-born generations (Alegría et al., 2008). Numerous studies have documented an association between later generation status and poorer mental health outcomes in both Latino youth (García Coll & Marks, 2012) and adults (Alegría et al., 2008; Grant et al., 2004). Peña et al. (2008) found that, compared to 1st-generation Latino youth, 2nd-generation Latino youth were more than twice as likely to attempt suicide, and 3rd-generation youth were more than three times as likely. Similarly, in a national sample, the

percentage of U.S.-born Latinas at risk for suicide was a quarter greater than the percentage of first-generation (immigrant) adolescent Latinas who reported STB (SAMHSA, 2003).

Generation status is not synonymous with acculturation, yet internalization of majority-culture values increases across generations, and there are associations between acculturation and STB in youth and young adults of some communities (Castle et al., 2011; Ng, 1996; Ortin et al., 2018). This may act through interpersonal processes, as later-generation youth often experience greater child-parent cultural dissonance, and resulting family conflict, as the youth may prefer certain U.S. majority culture attitudes or practices (Ying & Han, 2007). Conversely, first-generation youth often identify more with traditional family values (Canino & Roberts, 2001), which may reduce family conflict and buffer against the stresses associated with acculturation and assimilation (Cervantes et al., 2014). As Mexican-origin families continue to immigrate to the U.S. and stay for generations, examining whether the immigrant paradox is present for Mexican-origin youth will be important to inform both future research and current interventions.

Familism

Compared to Caucasian individuals of Western European descent, people of Mexican-origin and other Latino communities typically live within larger family networks, are more family-oriented, and have greater expectations of exchange and reciprocity among family members (Keefe, 1984; Mindel, 1980). A multidimensional construct, *familism* encompasses both the strong identification or bond with the nuclear and extended family, and feelings of familial loyalty and solidarity (Marín & Marín, 1991). A robust sense of familism, in which members greatly depend on one another for several needs, may buffer Latino adolescents from developing STB. Latino adolescents who report greater familism also report better mental health (Kapke et al., 2017; Stein et al., 2015) and suicide attempts are less prevalent among Latina youth who

reported tight-knit families with strong familism, compared to those who do not (Kuhlberg et al., 2010; Peña et al., 2011). Few studies have examined direct relations between familism on STB and, to date, studies have been cross-sectional, such that it remains unclear whether familism protects against STB over time.

Family Conflict

Family conflict is related to STB across cultures (Kuhlberg et al., 2010; Lau et al., 2002; Miller et al., 2012), and this form of interpersonal strain may create a particularly stressful environment for Latino adolescents. In many Latino cultures, the family unit is central to identity (Zayas et al., 2005) and fissures within the family can destabilize the developing youth's sense of self-worth, security, and predictability. Latino adults who reported negative family interactions and less family cohesion while growing up were more likely to report also experiencing suicidality before the age of 18 (Fortuna et al. 2007). Similarly, in a study of Latino youth, greater adolescent-parent conflict was associated with suicide attempts, although this relation was mediated by self-esteem and internalizing behaviors (Kuhlberg et al., 2010).

There is abundant research documenting the association between family conflict and adolescent STB across all communities (Asarnow & Carlson, 1988; Brent et al., 1994; Carballo et al., 2020; Fergusson & Lynskey, 1995). In a sample of Asian American children and adolescents, participants who reported high parent-child conflict were nearly 30 times more likely to engage in suicidal ideation and/or self-harm, compared to their peers who reported lower levels (Lau et al., 2002). Prinstein and colleagues (2000) reported a concurrent link between adolescent reports of overall family dysfunction and increased suicidal ideation in a clinically high-risk sample of 12- to 17-year-olds, with effect sizes nearing medium magnitude. Similarly, DeVille et al. (2020) found that in a sample of approximately 12,000 9- and 10-year-

old children, those living in high-conflict families were more likely to report suicidal ideation and/or to have attempted suicide compared to peers living in lower conflict families. This association held after controlling for family history of depression and suicidality, financial adversity, and parent-reported child internalizing and externalizing problems, suggesting that dysfunction within the parent-child relationship may be specifically relevant for identifying risk for STB. However, with a paucity of longitudinal research examining associations between family conflict and STB in Latino populations, it is unclear whether family conflict is a prospective risk factor contributing to the development of suicidality in Latino adolescents. Given the centrality of the familial unit within Latino communities, including the Mexican-origin population, experiences of family conflict warrant longitudinal examination.

Peer Conflict

The quality of peer relationships is also an important predictor of adolescent suicidality (Grudnikoff et al., 2015; Prinstein et al., 2000). Interpersonal stressors, such as being bullied or excluded by peers, are commonly reported by youth who also engage in STB (Cheek et al., 2020; Juvonen & Graham, 2014; King & Merchant, 2008; Winsper et al., 2012). More conflict with peers has been associated with a greater likelihood of endorsing STB in Latinas, specifically (Romero et al., 2013), and both Latino and Latina adolescents who reported peer victimization at school evinced higher levels of suicidality, compared to their peers who did not report being victimized (Robinson et al., 2021; Villarreal-Otálora et al., 2020). In a cross-cultural meta-analysis, Van Geel and colleagues (2014) found a robust, concurrent association between peer victimization and adolescent STB across dozens of studies; yet the authors also noted the lack of prospective research. Thus, greater conflict with peers is a risk factor for STB in Latino youth,

yet it remains an open question whether, and at what age, experiencing peer conflict constitutes a specific risk factor for the onset of STB in Mexican-origin youth.

Biological Sex

STB are more prevalent among adolescent girls of all ethnic groups, compared to adolescent boys (Kann et al., 2014, 2018; Rich et al., 1992), especially Latinas (Kann et al., 2014; Price & Khubchandani, 2017; Rasmussen et al., 1997; Villarreal-Otálora et al., 2019; Zayas et al., 2005). Across extant studies, rates of completed suicides for adolescent girls are lower than those for adolescent boys in several industrialized countries, but suicidal ideation and attempts follow an opposite trend (Fergusson et al., 2000; Grunbaum et al., 2004). That is, although girls may be less likely to die by suicide, they are more likely to endorse suicidal ideation and engage in non-lethal suicidal behaviors (Lawson et al., 2021; Orri et al., 2020; Rich et al., 1992). This well-documented sex gap may widen when examining ethnic minority populations. Across epidemiological studies, adolescent Latinas have steadily evinced elevated rates of STB, higher than their male counterparts as well as adolescents of most other ethnicities (Querdasi & Bacio, 2021). In the U.S., an estimated 15.6% of Latina adolescents have attempted suicide one or more times (CDC, 2013); until recently, this problem garnered little attention in the medical or mental health fields (Nock et al., 2013).

Development of STB in Adolescence

Most longitudinal research on adolescent STB has used predominantly Euro-American samples, neglecting the ethnic and racial diversity of youth in the U.S. Studies of the developmental course of STB have found that suicidality increases, on average, from early to late adolescence, with moderate to high rank-order stability, indicating that prior suicidality predicts future suicidality (Carbone et al., 2019; Garrison et al., 1991; Orri et al., 2020; Steinhausen et al.,

2006). Suicidal ideation peaks around age 15 (Rueter & Kwon, 2005), near the transition into high school. Similarly, epidemiological data suggest that the highest rate of STB occurs between 12 and 17 years of age (Nock et al. 2013). Together, these studies suggest that adolescence represents a uniquely vulnerable window for STB, and recent national data (Ivey-Stephenson et al., 2020; Ruch et al., 2019) indicate that suicidality is on the rise in this age group with no signs of abating, but less is known about the developmental course of suicidality in Latino youth.

In our prospective study of Mexican-origin youth, we conducted annual assessments of STB beginning at age 10. Our first paper on STB in Mexican-origin youth (Lawson et al., 2021) documented increases over early adolescence that peaked between 14 and 15 years, mirroring the developmental trajectory of adolescent STB in other ethnic groups (Nock et al., 2013). Focused on temperamental predictors of STB, that study revealed that effortful control was associated with decreased probability of STB by Mexican-origin youth whereas negative emotionality (e.g., aggression, frustration, depressed mood) was associated with increased likelihood of STB. In the current investigation, we examined the degree to which six salient risk and protective factors predicted the onset and developmental course of STB in Mexican-origin youth.

The Present Study

The current work focused on psychosocial predictors specific to the lives of Mexican-original youth across their adolescent years, from 10 to 17 years. Most prior research on the predictors of STB in Latino youth have been cross-sectional examinations of concurrent associations (i.e., Cardoso et al., 2018; Kann et al., 2018; Piña-Watson et al., 2014), or brief longitudinal studies of 1-2 year durations (i.e., Roche et al., 2020). Additional longitudinal repeated-measures studies across adolescence are required to inform interventions with Mexican-origin youth, because it is unknown whether multiple psychosocial factors differentially predict STB at particular points in

adolescence. Therefore, using an 8-year prospective design, the current investigation aimed to: (1) measure the onset and growth of STB in Mexican-origin youth across the adolescent years; and (2) examine which factors contribute to presence versus absence of STB at different points of adolescent development.

We hypothesized that within our sample of Mexican-origin adolescents: (1) females youth would evince a faster rate of increasing STB over adolescence, compared to males; (2) later generation youth would evince a faster rate of increasing STB over adolescence; (3) greater family conflict, peer conflict, and ethnic discrimination would be concurrently and prospectively associated with reporting STB; and (4) greater familism would act as a protective factor, decreasing the prevalence of reported STB concurrently and prospectively. These risk and protective factors were assessed repeatedly across adolescence, but due to the scarcity of prior developmentally informed research, we did not pose *a priori* hypotheses about whether they would be associated with STB more versus less strongly at different ages.

Method

Participants

This study used data from the California Families Project (CFP), a longitudinal study of 674 Mexican-origin youth (50% female) in Northern California focused on predicting the emergence and development of substance use. Youth were drawn at random from the 2006-2007 and 2007-2008 school rosters of 5th grade classrooms in one large (population > 450,000) city and one small (population < 60,000) city that served adjacent rural areas. The majority of the students enrolled in these two school districts were Latino (i.e., 53% Latino, 20% White, 11% Asian, 10% African American, and 6% other racial or ethnic backgrounds). Youth and parent participants self-identified as being of Mexican heritage, and youth were 29% first-generation (born in

Mexico, immigrated to U.S.), 62% second-generation (born in U.S. to parents who immigrated to U.S.), and 9% third-generation (grandparents were born in Mexico and immigrated to U.S.). Most families were two-parent households (82%), with gross annual household income ranging from less than $5000 to more than $95,000, measured in $5,000 increments (*M* = $32, 500). Annual family income was converted into income-to-needs (ITN) ratios based on family size. Parents provided informed consent for their child's participation, and youth provided assent. This study was approved by the university's Institutional Review Board.

Youth were assessed annually from 5th (M_{age} = 10.86, *SD* = 0.50) through 12th grade (M_{age} = 17.73, *SD* = .52). Retention was high, based on youth who participated in 3 or more years of data collection (94.8%; *N* = 639). The sample *N*s for each assessment were: Grade 5, *N* = 674; Grade 6, *N* = 569 (84.4%); Grade 7, *N* = 578 (85.8%); Grade 8, *N* = 591 (87.7%); Grade 9, *N* = 605 (89.8%); Grade 10, *N* = 590 (87.5%); Grade 11, *N* = 600 (89.0%); and Grade 12, *N* = 600 (89.0%). No youth were lost due to suicide or other causes of death during this period.

Procedures and Measures

Trained research staff interviewed participants in their homes in either Spanish or English, based on participant preference. Interviewers were all bilingual and most were of Mexican heritage. To ensure discretion and given the sensitive nature of the STB questions, youth responded to the measures assessing STB without the help of the interviewers (i.e., youth reported their responses directly on a computer that was turned away from interviewers), apart from the administration of a clinical interview that was implemented as a part of the larger CFP study, discussed below.

Suicidal Thoughts and Behaviors

To measure participants' STB, two different instruments were used: the NIMH Diagnostic Interview Schedule for Children (DISC-IV; Shaffer et al., 2000) and a brief suicide questionnaire adapted from the Youth Risk Behavior Survey (Brener et al., 2013). The DISC-IV is a fully structured diagnostic interview designed for use by non-clinicians to measure common psychiatric symptoms for diagnoses in children (Shaffer et al., 2000). In the annual assessments from 5th through 12th grade, youth responded (0 = *no*, 1 = *yes*) to two DISC-IV items assessing STB, i.e. "Was there a time when you thought seriously about killing yourself?"; "During the last year, have you tried to kill yourself?". The suicide questionnaire was administered annually from 6th through 12th grade and included three self-report items; i.e. "Have you thought about committing suicide?"; "Have you made a plan for committing suicide?"; "Have you attempted suicide?" (1 = *never*, 2 = *once*, 3 = *twice*, 4 = *3 or more times*).

After visits were completed and interviews were examined by research staff, parents were contacted if youth reported having any imminent thoughts of self-harm and/or suicide. Although study questions did not specifically probe for imminent risk, if youth spontaneously reported active suicidality, research staff contacted caregivers and made appropriate referrals.

A dichotomous STB score was derived from the two DISC-IV items in 5th grade plus the three additional items in all subsequent years. Participants' affirmative responses to one or more of the items were scored as 1 ("yes") for STB at that grade. Participants responding "never" or "no" to all items were scored as 0 ("no") for STB at that grade. The intra-class coefficient for the five items used to generate the final STB score ranged from α = .66 - .78 (M_{α} = .73)

Psychosocial Predictors

Each psychosocial predictor variable was measured by youth self-report at grades 5, 7, 9, and 11, allowing for concurrent and prospective predictions of how each factor may uniquely exacerbate or mitigate participants' STB across adolescence.

Family Conflict and Peer Conflict. Conflict with family and conflict with peers were assessed using two subscales from the Multicultural Events Scale for Adolescents (MESA; Gonzales et al., 1995). To measure family conflict, participants answered "yes" (1) or "no" (0) to nine items assessing recent (i.e., past three months) negative interactions with caregivers, i.e., "You had a serious disagreement or fight with a parent" (mean coefficient alpha across grades ranged from α = .56 - .69, M_α = .64). To measure peer conflict, participants answered "yes" (1) or "no" (0) to 14 items assessing recent negative life events involving peers, i.e., "Other kids said mean or bad things to you" (α = .60 - .73, M_α = .67). For each scale, responses were averaged at each grade such that higher scores indicated greater conflict (possible range 0.0 – 1.0). Given the MESA is a checklist of individual events, test-retest reliability may be a better indicator of internal validity and test-retest correlations for a two-week period demonstrated strong reliability for the complete measure (*rs* = .69 - .81; Gonzales et al., 1995).

Ethnic Discrimination. Ethnic discrimination was measured using six items from the Adolescent Perceptions of Discrimination scale (Johnston & Delgado, 2004), which assessed discrimination specifically targeted at Mexicans and Mexican-Americans in the school setting (e.g., "You have heard kids at school making jokes or saying bad things about Mexicans or Mexican-Americans"). Participants rated each item from 1 ("not at all true") to 4 ("very true"). Responses were averaged at each grade (α = .54 - .71, M_α = .63) with higher scores indicating more perceived ethnic discrimination (possible range 1.0 – 4.0).

Familism. Familism was measured using 16 items from the Mexican-American Cultural Values Scale (MACVS; Knight et al., 2010), assessing felt support, obligation, and need to defer to the nuclear family (e.g., "How much do you agree that parents should teach their children that the family always comes first?"). Participants rated each item from 1 ("not at all") to 4 ("very much"). Responses were averaged at each grade (α = .82 - .88, M_α = .86) with higher scores indicating greater familism (possible range 1.0 – 4.0).

Data Analytic Plan

To examine changes in STB over time and predict STB levels at each grade, we used latent growth curve (LGC) modeling (Bollen & Curran, 2006; McArdle, 2009). LGC models estimate within-person trajectories of growth as well as between-person differences in these trajectories. We examined if these trajectories were a function of time-invariant and time-variant theoretically derived predictors (Raudenbush et al., 2001). Observed STB across grades (5-12) were treated as a dichotomous dependent variable (1 = *yes*, 0 = *no*). Each STB measure was then used to create a latent variable at each grade representing a continuous latent response underlying the observed yes or no responses (Masyn & Petras, 2013). Changes in the latent variables across grades were examined with the LGC. All models were implemented in *Mplus* (Muthén & Muthén, 2018) using the weighted least squares-mean adjusted estimator (i.e., WLSM).

In the first set of LGC models, we tested no-growth, linear growth, and latent basis models to assess the trajectory that provided the best fit for STB across grades. Model fit was evaluated using four indices: (a) the chi-square goodness of fit test; (b) the comparative fit index (CFI; Bentler, 1990); (c) the Tucker-Lewis index (TLI; Tucker & Lewis, 1973); and (d) the root mean square error of approximation (RMSEA; Steiger, 1990). In these analyses, we did not include

ITN ratio as a covariate because preliminary analyses using zero-order correlations and SEM found that ITN ratios were not significantly associated with adolescent STB.

In the second set of LGC models, the goal was to examine the role of psychosocial factors. We included these variables first individually and then simultaneously. These variables were added as time-varying covariates to predict the latent factor representing STB concurrently (grades 5, 7, 9, 11) and prospectively (grades 6, 8, 10, 12), after accounting for the stability over time of STB. Therefore, each psychosocial predictor was examined for its concurrent association with STB, and for its prediction of increased or decreased STB in the subsequent year.

First, we examined four LGC models, including each psychosocial predictor separately to examine the individual contributions to changes in STB over time, while adjusting for sex and generation status as time-invariant covariates. Second, the four psychosocial predictors then were included within one LGC model to examine unique and additive contributions to STB, while adjusting for sex and generation status as time-invariant covariates.

Missing data ranged from 5%-16% in each year. To account for this, we used full information maximum likelihood (i.e., FIML). FIML is highly flexible in dealing with partially random missing data (Graham et al., 2007) and one of the most efficient and unbiased estimations techniques for missing data currently available (Enders & Bandalos, 2001). Little's (1988) MCAR test indicated that data were not missing completely at random, $\chi 2\ (638) = 756.21$, $p < .01$. Attrition analysis for multiple comparisons revealed no differences between participants who were present versus absent in Grade 12 across the 16 measures of focal variables. Missingness was not associated with demographic characteristics, such as socioeconomic status, generation status, or sex, indicating that the data conformed to missing at random (i.e., MAR; Enders, 2010) standards.

Results

Descriptive Statistics

Descriptive statistics for the prevalence of STB are reported in Table 1, and for psychosocial predictors in Table 2. STB increased from grades 5 (M_{age} =10.9 years) to 9 (M_{age} =14.8 years) and then was maintained at comparable prevalence through to grade 12 (M_{age} =17.7 years), with more girls than boys reporting STB from grade 6 onward. By grade 12, 27.7% of the total sample (38% of girls; 17.5% of boys) had endorsed STB at least once, and 13.7% (20.2% of girls; 7.5% of boys) had endorsed at two or more grades. Considering generation status, 16.8% of first-generation, 22.4% of second-generation, and 20% of third-generation youth had reported STB by grade 12. Figure 1 illustrates the proportion of participants who disclosed initial and/or reoccurring STB at each grade, and the cumulative proportion of participants who endorsed having a history of STB across the 8 grades.

Concurrent correlations between the time-varying predictors were computed for each year they were collected. Peer and family conflict showed the strongest correlations across each year they were collected, *rs* = .16 to .55, all $p < .001$. Experiences of ethnic discrimination were significantly and positively correlated peer and family conflict, *rs* = .08 to .41, all $p < .05$. The correlation between familism and family conflict ranged from $\underline{r}$s = -.23 to -.04 and was significant at Grades 7, 9, and 11, all $p < .01$. Overall, correlations between predictors were small to moderate in magnitude.

Changes in STB Across Time

LGC with no covariates

An unconditional non-linear growth curve estimating latent STB over time produced better model fit than the no-growth or linear-growth models, $\chi^2(24) = 34.46$, p =.08, CFI =.99,

Table 2.1 Summary Information on Participants' Reporting of Suicidal Thoughts and Behaviors (STB) at Each Grade

Grade	M_{age} (years)	Total *N*	Endorsed suicidality *N* (%)	Females endorsing *N* (%)	Males endorsing *N* (%)	Prior suicidality *N* (%)	Subsequent suicidality *N* (%)
5	10.9	642	18 (2.8)	8 (2.5)	10 (3.1)	-	7 (38.9)
6	11.8	565	26 (4.6)	16 (5.7)	10 (3.5)	3 (11.5)	19 (73.1)
7	12.8	577	33 (5.7)	25 (8.6)	8 (2.8)	17 (51.5)	26 (78.8)
8	13.8	591	40 (6.8)	32 (10.7)	8 (2.7)	17 (42.5)	25 (62.5)
9	14.8	605	73 (12.1)	55 (18.0)	18 (6.0)	28 (38.4)	52 (71.2)
10	15.8	590	56 (9.5)	42 (14.0)	14 (4.8)	35 (62.5)	35 (62.5)
11	16.8	600	77 (12.8)	57 (18.9)	20 (6.7)	50 (64.9)	38 (49.4)
12	17.7	600	66 (11.0)	46 (15.1)	20 (6.8)	52 (78.8)	-

Note. Values reported include total number and proportion reporting STB, number and proportion of females and males reporting STB, and number and proportion of youth reporting STB who had reported STB in the prior years, and who reported STB in the subsequent years.

Table 2.2 Regression Coefficients of Four Latent Growth Curve Models Predicting STB from 5th - 12th Grades

			Suicidal Thoughts and Behaviors							
	Grade		5th	6th	7th	8th	9th	10th	11th	12th
Predictor		*M* (*SD*)				*B* (*SE*)				
Family Conflict										
	5th	.08 (.13)	**1.81*** **(.77)**	.19 (1.27)	-	-	-	-	-	-
	7th	.07 (.12)	-	-	**3.07***** **(.44)**	.58 (.49)	-	-	-	-
	9th	.10 (.15)	-	-	-	-	**2.07***** **(.34)**	.65 (.50)	-	-
	11th	.10 (.15)	-	-	-	-	-	-	**1.53***** **(.40)**	**1.26*** **(.49)**
Peer Conflict										
	5th	.15 (.16)	**1.52*** **(.66)**	-.25 (2.04)	-	-	-	-	-	-
	7th	.48 (.34)	-	-	.02 (.17)	-.02 (.14)	-	-	-	-
	9th	.13 (.15)	-	-	-	-	**2.12***** **(.33)**	.43 (.49)	-	-
	11th	.12 (.14)	-	-	-	-	-	-	.83 (.51)	.48 (.56)
Discrimination										
	5th	1.40 (.40)	.26 (.12)	-.08 (.30)	-	-	-	-	-	-
	7th	1.25 (.31)	-	-	.20 (.15)	.05 (.12)	-	-	-	-
	9th	1.29 (.33)	-	-	-	-	**.41**** **(.12)**	.12 (.35)	-	-
	11th	1.30 (.31)	-	-	-	-	-	-	**.29*** **(.12)**	.22† (.12)
Familism										
	5th	3.63 (.31)	.13 (.28)	-.19 (.17)	-	-	-	-	-	-
	7th	3.60 (.34)	-	-	**-.45***** **(.09)**	**-.60***** **(.13)**	-	-	-	-
	9th	3.52 (.36)	-	-	-	-	**-.78***** **(.16)**	**-.81***** **(.15)**	-	-
	11th	3.44 (.39)	-	-	-	-	-	-	**-.77***** **(.16)**	**-.76***** **(.16)**

Note. STB = Suicidal thoughts and behaviors. Each model was predicted individually by family conflict, peer conflict, ethnic discrimination, and familism measured at 5th, 7th, 9th, and 11th grades. The regression coefficients presented in this table are unstandardized and represent the unit change expected in STB given a one-unit change in the key predictor of each model, concurrently (i.e., 5th to 5th) and one year subsequently (i.e., 5th to 6th). Means and standard deviations reported are unstandardized values. Sex and generation status were included in each model and slopes were specified to show STB growth from grades 5-9 and STB stability from grades 10-12. Model fit was excellent and had the following range of values: $\chi^2(65) = 80.68 - 138.01$, $.0001 < p < .09$, CFI =.97 – 1.0, TLI = .96 – 1.0, RMSEA = .01 - .04. Significant effects are in bold font, with significance levels denoted as $*p < .05$, $**p < .01$, $***p < .001$.

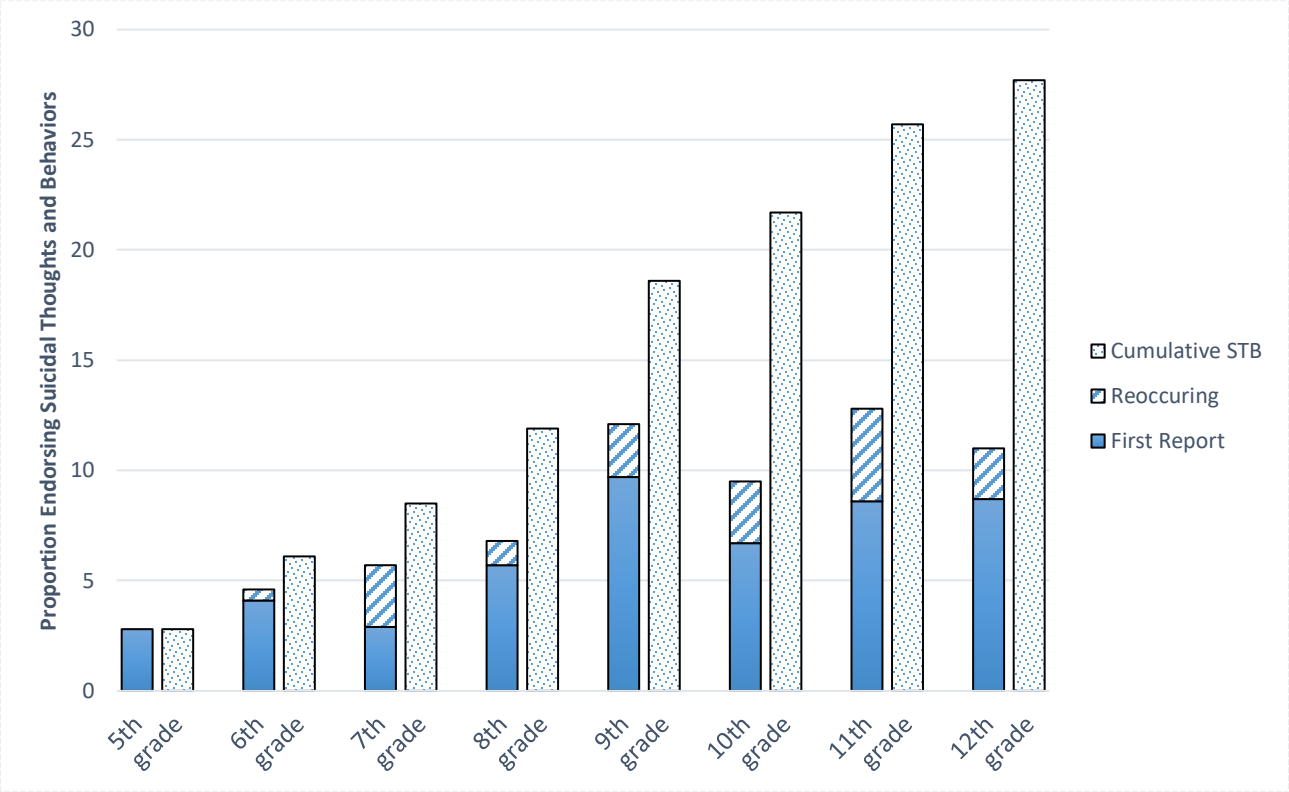

Figure 2.1 Proportion of participants endorsing a history of STB at grade 5. STB was measured annually, and history of STB was not collected prior to 5th grade. Reoccurring and first report represent the total proportion of participants who endorsed STB at that grade. Cumulative STB represents participants who endorsed at the current or prior grade. Proportions represent the valid percentage, based on the number of participants at each grade. See Table 1 for *N*s at each grade. STB = Suicidal thoughts and behaviors.

TLI=.99, RMSEA=.03 (see Figure 2). This model yielded a linear increase in STB from 5th to 9th grade followed by stability of the prevalence of STB across the remaining grades. The positive estimate of the slope mean (M_{slope} = .09, *SE* = .02, $p < .0001$) together with the slope loadings [λ = 0,1,2,3,4,4,4,4] indicated that individual STB significantly increased over time until grade 9 and then stabilized. Given the intercept was fixed to zero, as an arbitrary initial STB status, these changes can be interpreted as departing from zero. The variance around the mean slope was statistically significant ($p < .05$), indicating there was notable variability across participants in the development of STB from grades 5 to 12.

LGC with Sex, Generation Status, and Time-variant Predictors

Psychosocial factors at grades 5, 7, 9 and 11 were first entered independently into four separate single-predictor models (see Table 2) and then jointly into one multi-predictor model (see Table 3) to examine concurrent and prospective unique and additive contributions to STB, respectively. Here, the predictors were related to the latent factor representing STB. In addition, autoregressive paths for STB were also included to control for the year-to-year stability of STB, and sex and generation status were retained in all models. All time-varying and time-invariant predictors were allowed to co-vary in each model.

As presented in Table 2, when examined individually, each psychosocial predictor was concurrently associated with STB in at least two of four grades, and family conflict and familism were prospectively predictive of STB in one or more subsequent grades. The number and magnitude of associations increased across grades, as more adolescents reported STB. Family conflict and familism demonstrated the greatest numbers of significant paths predicting both concurrent and subsequent STB. The directions of all associations were in accord with predictions: more family and peer conflict, and more ethnic discrimination predicted higher

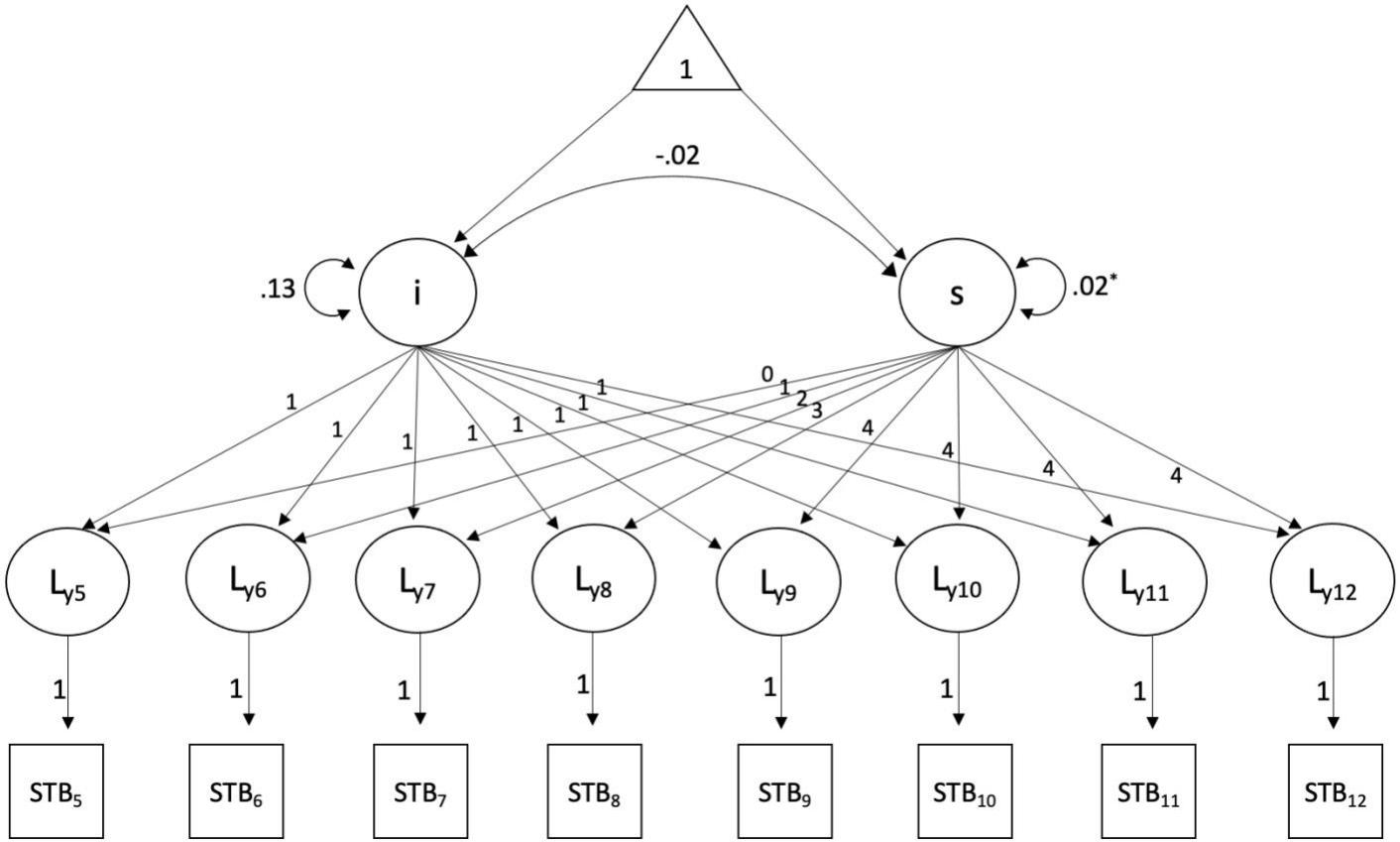

Figure 2.2 Results of an 8-wave non-linear unconditional latent growth curve model of Mexican-origin youth suicidal thoughts and behaviors from grade 5 to grade 12. STB = suicidal thoughts and/or behaviors. Significance levels are denoted as: *$p < .05$. The slope and intercept variances and covariance reported represent unstandardized results.

Levels of STB, whereas greater familism predicted lower levels of STB. Across the models with individual predictors, generation status was a significant predictor of the slope in every model, and sex was a significant predictor of the slope in two of the four models, with later generation and female youth evincing steeper STB slopes. Each single-predictor model had excellent model fit (for specific indices, see Table 2).

As presented in Table 3, when psychosocial predictors were examined simultaneously within one LGC model, family conflict and peer conflict significantly and positively predicted STB both concurrently and prospectively, whereas familism significantly and negatively predicted STB concurrently and prospectively. Family conflict and familism predicted STB across most grades; peer conflict in 9th grade was specifically linked to greater STB in 9th and 10th grades. In contrast, ethnic discrimination was not significantly related to STB at any age, after accounting for the other predictors. These effects were incremental and additive to the significant and positive effects for sex on the slope ($\beta = .07$, $SE = .03$, $p < .05$), generation status on the slope ($\beta = .06$, $SE = .02$, $p < .01$), and year-to-year stability of STB from grades 6 through 11 (βs = .33 - .54, SEs = .09 - .14, all ps < .05 - .0001). Female and later generation participants had steeper trajectories of increasing STB over time, compared to male and earlier generation participants. This model with all predictors entered simultaneously had excellent model fit (see Table 3 for specific indices).

To facilitate the interpretation of the path coefficients in Table 3, median splits were performed on the significant predictors in order to describe STB rates for youth reporting relatively higher versus lower values of the psychosocial measures. Note that these descriptive statistics are not direct translations of the path coefficients from the model but are provided to help convey the magnitudes of the effects identified. In concurrent associations, youth who

Table 2.3 Regression Coefficients of the Latent Growth Curve Model Predicting STB from 5th-12th Grades Predicted Jointly by Family Conflict, Peer Conflict, Ethnic Discrimination, and Familism

		Suicidal Thoughts and Behaviors							
Grade		5th	6th	7th	8th	9th	10th	11th	12th
	Predictor	*B* (*SE*)							
5th	Family Conflict	**1.80* (.60)**	-2.21 (1.99)	-	-	-	-	-	-
	Peer Conflict	.56 (.70)	1.41 (1.24)	-	-	-	-	-	-
	Discrimination	-.07 (.20)	.53 (.38)	-	-	-	-	-	-
	Familism	.13 (.29)	-.36 (.32)	-	-	-	-	-	-
7th									
	Family Conflict	-	-	**2.84*** (.44)**	.89 (.73)	-	-	-	-
	Peer Conflict	-	-	-.18 (.22)	.15 (.20)	-	-	-	-
	Discrimination	-	-	.35 (.24)	-.14 (.23)	-	-	-	-
	Familism	-	-	**-.38*** (.11)**	**-.32** (.11)**	-	-	-	-
9th									
	Family Conflict	-	-	-	-	**1.35** (.44)**	.21 (.50)	-	-
	Peer Conflict	-	-	-	-	**1.05* (.51)**	**1.21*(.55)**	-	-
	Discrimination	-	-	-	-	.03 (.18)	.004 (.19)	-	-
	Familism	-	-	-	-	**-.46*** (.12)**	**-.49*** (.13)**	-	-
11th									
	Family Conflict	-	-	-	-	-	-	**1.37** (.44)**	**1.39** (.47)**
	Peer Conflict	-	-	-	-	-	-	.33 (.63)	.46 (.62)
	Discrimination	-	-	-	-	-	-	-.11 (.22)	-.23 (.22)
	Familism	-	-	-	-	-	-	**-.39** (.13)**	**-.36** (.12)**

Note. This model was predicted jointly by family conflict, peer conflict, ethnic discrimination, and familism measured at 5th, 7th, 9th, and 11th grades. The regression coefficients presented in this table are unstandardized and represent the unit change expected in suicidal thoughts and behaviors given a one-unit change in a given predictor while adjusting for the other predictors, concurrently and one year subsequently. Sex and generation status were included in the model. Model fit was excellent: $\chi^2(149) = 229.50$, $p < .0001$, CFI =.99, TLI = .97, RMSEA = .03. Significant effects are in bold font, with significance levels denoted as $*p < .05$, $**p < .01$, $***p < .001$.

reported lower familism had at least twice the prevalence of STB as youth who reported greater familism (Grade 7: 8.1% vs. 3.6%; Grade 9: 16.2% vs 7.8%; Grade 11: 18% vs. 8%); the opposite pattern was evident for less versus more family conflict (Grade 5: 1.1% vs. 5.4%; Grade 7: 1.6% vs. 13.8%; Grade 9: 6.6% vs 20.4%; Grade 11: 6.2% vs. 22.4%) and peer conflict (Grade 9: 6.1% vs 19.1%). These effects were mirrored in the prospective associations for familism (Grade 7 familism to Grade 8 STB: 7.2% vs. 5.2%; Grade 9 to 10: 12.9% vs 5.7%; Grade 11 to 12: 12.1% vs. 8%), family conflict (Grade 11 to 12: 4.1% vs. 21.6%) and peer conflict (Grade 9 to 10: 4.1% vs 15.6%).

Discussion

The emergence of STB during adolescence for Mexican-origin youth was driven by biological sex and generation status, as well as by their experiences of contentious family and peer relationships, and disconnection from the traditional Latino value of familism. More family conflict and less familism were predictive of subsequent STB across adolescence, whereas peer conflict appeared to be particularly pernicious in the mid-adolescence period. Whereas ethnic discrimination experiences at school predicted adolescent STB when considered individually, when examined in the context of the other family and peer relationship measures, it was not independently and additively associated with suicidality.

Recognizing the cultural significance of relational processes for STB risk is critical for public and mental health professionals working with Mexican-origin and other Latino youth and their families, many of whom may interface with community mental health providers. Despite being at an elevated risk for STB (Kann et al., 2018; Villarreal-Otálora et al., 2019; Zayas et al., 2005), Latino youth are underrepresented in studies of the predictors of STB, making these novel findings even more critical for efforts to address the youth mental health crisis. By identifying

the antecedent risk and protective factors that predict subsequent STB in Mexican-origin adolescents, this study builds on our prior documentation of the increasing prevalence of suicidal ideation, plans and attempts from early adolescence into emerging adulthood (Lawson et al., 2021), and reveals potentially actionable targets for sorely needed STB prevention and intervention efforts (Alegría et al., 2002).

There was both increasing STB across adolescence, with the emergence of new cases annually, and marked stability in youth reporting STB from year to year. Cumulatively, STB had been reported by almost 30% of Mexican-origin youth by 12th grade. The prevalence of STB increased more quickly in girls than boys, and more than twice as many females as males reported STB at least once over adolescence. Similarly, in accord with the immigrant paradox model (Alegría et al., 2008; Peña et al., 2008), STB increased more quickly and were markedly more prevalent for youth of later generation status, compared to first-generation youth. All first-generation youth included in this study had immigrated to the U.S. by age 10 and, thus, we might have observed even stronger effects for generation status had our sample included participants who had immigrated after their 10th birthday, as some scholars have theorized that children who immigrate at a very young age may closer resemble second-generation youth (Perlmann, 2005).

Although the developmental course of suicidality appeared to mirror that of other ethnic and racial adolescent populations, other studies using community samples found lower lifetime prevalence rates of STB (Orri et al., 2020; Rueter & Kwon, 2005) compared to those present in this sample. Such an increase in suicidality across development for Mexican-origin youth, especially for girls and U.S.-born adolescents, calls for an expansion of universal screening in environments in which these adolescents are most likely to encounter mental or physical health services, such as schools and healthcare settings.

When considered annually, the proportion of middle and high school-aged Mexican-origin girls reporting STB in the past year was comparable to prior cross-sectional studies of U.S. Latina samples (Kann et al., 2014). Yet, such single time-point assessments of suicidality in the past year may underestimate the true prevalence, as we observed that by the time they were in 12th grade, 38% of girls had reported STB at least once since 5th grade, with 20% reporting STB across multiple years. These figures reinforce concerns that adolescent suicidality has reached epidemic levels in the U.S. (Hoffman et al., 2020), especially for Latinas (Price & Khubchandani, 2017; Zayas et al., 2005).

Additionally, the prevalence of STB in this sample of Mexican-origin female adolescents, mirroring that of U.S. Latina STB rates more broadly, was higher than that observed for similarly aged females in Mexico (Borges et al., 2008). Combined with our finding that more U.S.-born Mexican-origin youth than first-generation youth reported STB (Peña et al., 2008; SAMHSA, 2003), there is strong evidence that the U.S. national context is contributing to this public health problem for Mexican-origin adolescents. Our data were collected from 2006 through 2014, which was a period of increasing deportations for Latino communities (Gonzalez-Barrera & Krogstad, 2016), yet it preceded the rapid escalation in anti-immigrant political rhetoric, detainment and deportation that began in 2016 and has been linked to STB in Latino youth (Roche et al., 2020). Although we did not assess youth perceptions of the national context for Mexican-origin families, these factors may have played a role in their mental health. As the direct experience of discriminatory actions from peers and teachers did not account for these elevated rates of STB, further examination is needed to comprehensively understand the mechanisms behind the links between later generation status and increased risk for STB (but see Marks et al., 2014).

Corroborating findings from prior studies (Lau et al., 2002; Van Geel et al., 2014; Villarreal-Otálora et al., 2020), adolescents who experienced more conflict with peers and family were more likely to report STB at multiple ages, both when either risk factor was examined independently, and when the psychosocial factors were considered collectively. The quality of close relationships with family and friends conveys robust influences on Mexican-origin youth well-being (CDC, 2004; Fortuna et al., 2007; Kuhlberg et al., 2010; Piña-Watson et al., 2014; Zayas & Pilat, 2008). The transition into high school, 9th to 10th grade, was a particularly salient period for the effects of peer conflict, which has previously been noted as a vulnerable age for stressors to trigger suicidality (Kann et al., 2018; Rew et al., 2016). School-based prevention and intervention programs that target peer stressors might yield the greatest benefit by focusing on periods of academic transition, which can disrupt existing relationships and social support systems, and reduce social status relative to older youth in the new school setting (Goldstein et al., 2015; Magson et al., 2021). Furthermore, with less adult supervision, the transition to high school may make some youth more susceptible to peer victimization and, thus, place them at greater risk for STB.

The Mexican-origin youth in our study reported low rates of ethnic discrimination at school, which may have been attributable to the fact that most attended majority-Latino schools. Additionally, the measures of ethnic discrimination and peer conflict were positively correlated. Peer conflict and bullying directed at immigrant and ethnic minoritized youth often emphasizes differences in racial and ethnic background, language, and immigration status (Maynard et al., 2016; Peskin et al., 2007). This ethnic- or race-focused bullying could also be categorized as discrimination or racism, making this type of peer conflict especially noxious. It will be important for future research with Mexican-origin youth to contrast school and community

contexts in which they experience numeric minority or majority status, and to measure perceptions of both discriminatory and non-discriminatory peer conflict, to disentangle the unique contributions of each risk factor to STB.

It was the familial measures, though, that most strongly predicted STB by Mexican-origin adolescents, with family conflict exacerbating risk and familism values mitigating it. Additionally, at multiple points in adolescence, both lower familism and greater family conflict were associated with increased risk for suicidality one year later, an important extension from previous cross-sectional and retrospective research (Kuhlberg et al., 2010; Prinstein et al., 2000). Relatively few empirical studies have evaluated how familism is connected to more salubrious outcomes in adolescents (Schriber et al., 2017). Researchers have argued that Latino individuals with high levels of familism exhibit collectivistic values, showing an enduring responsibility for the well-being of their families beyond that of the self (Cauce & Domenech-Rodriguez, 2002). This greater focus on the needs of close others may keep Mexican-origin adolescents from engaging in STB because of heightened awareness of the impact of their own actions on their family members.

Negative relationship processes, particularly within the family, were key indicators of exacerbating STB. Arguing with caregivers and being critiqued by family members for not participating in traditional cultural events or showing pride in their Mexican heritage, were events captured by our measure of family conflict. This combination of relationship and cultural stressors within the family context may leave Mexican-origin adolescents feeling isolated from their primary support systems, making them especially vulnerable for STB. In line with the cultural value of familism, the Latino family structure and connections among family members are thought to facilitate and strengthen individual well-being (Alegría et al., 2002), but this

protective buffer may be disrupted by high levels of family conflict. The consistent, sustained, and predictive associations of familism and family conflict with STB suggest that focusing on family tensions and connections could be promising targets of prevention and intervention efforts to reduce adolescent STB in the Mexican-origin community (Goldston et al., 2008), as well as promoting cultural identification to foster connectedness and support well-being (Berkel et al., 2010). The stability with which greater familism predicted decreased STB across adolescence highlights the protective role of family connectedness and cultural identification for Mexican-origin youth (Ayón et al., 2010; Cruz et al., 2019; Schriber et al., 2017), even in the face of conflict and adversity in other realms of the adolescent's life. Knowing the extent to which family processes play critical roles in promoting or undermining Mexican-origin adolescents' mental health, future prevention and intervention efforts should leverage these cultural values to foster greater family connectedness and support caregivers to navigate conflict with their adolescents.

It should be emphasized that although all the psychosocial factors demonstrated independent and/or unique contributions to greater youth STB, within this unselected community sample, most participants did not endorse high levels of family conflict, peer conflict, and ethnic discrimination. Despite evincing lower variability and modest levels of risk, the analyses still demonstrated that even moderate adversity across different realms of life, especially involving interpersonal relationships, can lead to worse mental health outcomes for Mexican-origin youth. Presumably, rates of STB could be even higher in Mexican-origin and other Latino youth who experience more severe psychosocial adversities.

Limitations and Future Directions

By collecting repeated measurements of STB and its psychosocial predictors across adolescence and utilizing LGC modeling techniques to assess change over time in suicidality, this study provides vital insights for mental health researchers and practitioners working with the rapidly growing but understudied Mexican-origin community. Yet, as with all research, our findings must be considered within the context of certain study limitations.

First, in recognizing the diversity of the broader Latino community (Noe-Bustamante, 2019), and the structural and contextual differences in life circumstances for Latino families across the U.S. (Landale et al., 2006), it is important to acknowledge that these data were collected from the Mexican-origin population in California, and thus may not reflect the experience of other Latino adolescents or even Mexican-origin communities in other U.S. states. Second, all measures of STB and psychosocial predictors were derived from youth self-report. It would be beneficial for future research to also include reports by either parents or teachers, who would offer distinct accounts of youth's behavior or adverse experiences. Third, some of our psychosocial questionnaires measuring negative events and interpersonal adversity produced modest internal consistency. This may be attributed to the relatively low prevalence of reported ethnic discrimination and interpersonal conflict among the participants, but in addition, these were formative constructs for which high inter-item correlations are not expected, such that metrics of internal consistency like coefficient alpha are not ideal (Bollen & Bauldry, 2011; Bollen & Lennox, 1991; Markus & Borsboom, 2013). Despite lower variability among these measures, significant associations with concurrent and prospective STB were identified. Fourth, our study was conducted from 2006 to 2014 and findings should be recognized as pertaining to that socio-historical period in the U.S. Forthcoming research would benefit from assessing youth

perceptions of the national context for Mexican-origin families over the recent years of increasingly vitriolic public discourse, and governmental policies and practices that have adversely affected this community. Given that the political climate and attitudes toward immigrants in the U.S., especially those from Mexico and Central America, has deteriorated since these data were collected (Lopez et al., 2018), it is likely such a hostile and pervasive environment will have enduring adverse influences. Factors such as national policies, structural inequities and systemic racism are likely to contribute to STB among Mexican-origin youth and youth from other marginalized populations (Roche et al., 2020; Nazroo, 2003), and these warrant further attention. Lastly, we recognize that suicidality is a multifactorial phenomenon which includes several contributing factors across domains, such as physiology, temperament, and other areas of psychopathology. While this study examined prominent psychosocial and cultural variables known to contribute to risk for STB (i.e., interpersonal conflict, ethnic discrimination), future research should include models that include multiple levels of analysis (e.g., Gene x Environment moderation) to capture both internal mechanisms and external influences.

Conclusion

Although decades of research have examined factors associated with adolescent STB, many questions remain about how to successfully identify which youth are at greatest risk and, consequentially, how to design efficacious prevention programs, especially for Mexican-origin and other Latino communities. By longitudinally assessing suicidal ideation, planning, and past attempts in a non-clinical Mexican-origin sample from early to late adolescence, our study demonstrated that normative youth experiences (e.g., fights with friends, difficulty with caregivers), even at modest levels, may be associated with experiences of suicidality at different points in development. Conversely, our work also suggests that experiences of connectedness to

family and having a sense of familial obligation may promote greater mental health in Mexican-origin youth and thus buffer against psychopathology. Finally, we identified demographic factors (increased age, female sex and generation status) that signaled risk for STB across adolescence, which could be targeted in prevention efforts such as screening strategies.

No single known predictor has been identified that leads a youth to experience suicidal ideation or make a suicide attempt, but the more research can illuminate various risk factors which make a youth vulnerable for suicidality, the closer developmental and clinical scientists come to understanding this complex phenomenon. In conclusion, as researchers and practitioners seek to develop efficacious interventions for adolescent STB, attention must be paid to the cultural values and relationship contexts of Mexican-origin and other Latino youth. Efforts to resolve tensions within the family and to promote Mexican-origin adolescents' connectedness to their families and culture across development may help stem the rising tide of adolescent suicide in the U.S.

CHAPTER THREE

STUDY 2: AUTONOMIC CORRELATES OF PAST AND PROSPECTIVE SUICIDAL THOUGHTS AND BEHAVIORS IN MEXCAN-ORIGIN YOUTH

Background

Suicide is the second leading causing of death for adolescents in the United States (Heron, 2019) and rates are increasing (Hoffman et al., 2020). Suicidality (i.e., having suicidal thoughts, making plans, and/or attempting suicide) disproportionately affects communities of color (Ivey-Stephenson et al., 2020; Kann et al., 2018), including Latino youth (Khan et al., 2018; Miron et al., 2019; Twenge et al., 2019). Research on potential physiological biomarkers of adolescent suicidality has predominantly been cross-sectional and utilized White, European-American samples. There have been few longitudinal studies examining the development of suicidal thoughts and behaviors (STB) in Mexican-origin youth in the U.S (Gonzalves et al., in press; Lawson et al., 2021), and none including neurobiological predictors of future STB. Social exclusion paradigms have been used to induce moderate stress in adolescents (Mwilambwe-Tshilobo & Spreng, 2021) and allow researchers to study differences in physiological stress responses between youth with and without STB (Kaufman et al., 2018). This prospective study on autonomic stress responses to social exclusion and STB in Mexican-origin youth was conducted to address the current gaps in the literature.

The Roles of the ANS

The need for more research on proximal risk factors for adolescent STB, including physiological indicators of acute stress dysregulation, has been highlighted (Miller & Prinstein, 2019). The autonomic nervous system (ANS) is responsible for the body's automatic and unconscious responses to the external environment and includes the parasympathetic (PNS) and

sympathetic (SNS) branches, measurable via such indices as respiratory sinus arrhythmia (RSA) and skin conductance responses (SCR), respectively. SNS activation increases somatic arousal, preparing the body for assertive or defensive action through reaction or retreat (i.e., "fight or flight"; Hastings & Kahle, 2019). The PNS, acting primarily via the vagus nerve, referred to as the "rest and digest" system, supports multiple responses and functions including calming, regulation, orientation, and engagement (Hastings & Kahle, 2019). Adolescents' basal and acute stress responsive ANS physiology is theorized to facilitate different autonomic strategies for addressing environmental demands, such that youth who fail adequately respond to challenges and cope with stress may be vulnerable to developing STB (Miller & Prinstein, 2019).

Parasympathetic and sympathetic arousal influence how individuals respond to environmental stressors, including their ability to cope with perceived challenges and threats (Porges, 2007; Hastings & Kahle, 2019). Higher tonic RSA and moderate withdrawal of parasympathetic influence (slight decrease in RSA) in reaction to aversive stimuli are associated with better emotion regulation (Beauchaine, 2015; Hastings et al., 2014; Miller & Prinstein, 2019), whereas lower tonic RSA and stronger (greater decrease in RSA) and weaker RSA withdrawal (no decrease, or increased RSA) are associated with emotion dysregulation (Beauchaine 2015; Beauchaine et al., 2007) and psychopathology (Beauchaine, 2012; Vasilev et al., 2009). SCR, measured via electrodermal activity, increases in arousal states associated with stress, affect, and attention (Gualniera et al., 2021). Mild sympathetic arousal leads to increased vigilance to environmental cues whereas a "fight or flight" response follows greater arousal (Hastings et al., 2007). Disproportionate responses of sympathetic arousal, whether over- or under-arousal, impair an individual's capacity to cope effectively with their present situation

(Keller, Hicks, & Miller, 2000) and have been associated multiple mental health issues including anxiety and depression (Asbrand et al., 2017; Blechert et al., 2007).

The ANS has been conceptualized as a negative-feedback homeostatic regulatory system, in which the SNS acts as an accelerator and the PNS as the brake, but modern theory posits that contributions of PNS and SNS on autonomic activation may act reciprocally, coactively, or even independently (Bertnson, Cacioppo, & Quigley, 1993). In his Polyvagal Theory, Porges (1995) conceptualized the PNS as a crucial factor of the social engagement system (Porges & Furman, 2011). He theorized that in a moderately stressful environment, modest SNS activation (i.e., increased SCR) paired with mild PNS withdrawal (i.e., decreased RSA) is considered adaptive, allowing for an individual to actively engage with the present stressor while maintaining effective regulation (Hastings & Kahle, 2019; Porges, 2007). Examining the relative contributions of each ANS branch to an individual's stress response is necessary to reveal the somatic sequelae of how that person perceives a particular stimulus and mobilizes resources in support of responses that may be adaptive or maladaptive (Berntson et al., 1993).

ANS and STB

To date, dominant neurobiological models of STB risk have been based on studies of adults and are not developmentally informed (Joiner et al., 2005; Ludwig et al., 2017). Considering ANS correlates of suicidality, adults with STB have relatively lower tonic and blunted reactivity of the SNS and PNS, or ANS hypoactivity, compared to adults without STB (Chesin et al., 2020; McCall et al., 2022; Smith et al., 2020; Thorell, 2009). For example, in studies of PNS activity and STB in adults, lower baseline high-frequency heart rate variability (HF-HRV) has been associated with both suicidal thoughts and attempts (Rottenberg, 2007; Wilson et al., 2016). Additionally, a recent study found that college-aged adults with a history of

suicidal ideation evinced less HF-HRV reactivity (less PNS decrease) in response to the Cyberball social exclusion task and a Stroop task, compared to peers without suicidal ideation (Chesin et al., 2020). Regarding the SNS, a meta-analysis led Thorell (2009) posited that electrodermal activity (EDA) hyporeactivity may be a biomarker of both prior and subsequent suicidality, including eventual death by suicide. Similarly, Sarchiapone and colleagues (2018) concluded that tonic and phasic EDA hypoactivity marked increased risk for STB. SNS hypoactivity may be related to an unconscious diminishment of environment awareness (Thorell et al., 2013), and a failure to mobilize physiological resources to meet outside demands (Sarchiapone et al., 2018). In the child research, sympathetic under-arousal has been connected to the emergence of externalizing problems (e.g., callousness, acting out; Cappacdocia et al., 2009), and low behavioral inhibition (Beauchaine, 2001). The stimulation-seeking theory suggests that low sympathetic activity (often indexed by EDA) is an unpleasant sensation and, thus, youth may be motivated to engage in disruptive behavior with the aim of increasing arousal (Cappadocia et al., 2009; Raine et al., 1997). The mechanism that connects low SNS to increased risk for STB is not well understood but the field has established that an underperforming ANS exacerbates risk for psychopathology, in general.

The limited psychophysiological research on STB in adolescents is not entirely consistent with the patterns observed in adults. In adolescents, prior history of STB has been associated with lower baseline RSA (Crowell et al., 2005), greater decreases in RSA (strongly reduced PNS activity) in response to a sad film clip (Crowell et al., 2005), but also less decrease in RSA using puzzle and discussion tasks (maintenance of PNS activity; James et al., 2017; Yang et al., 2019), compared to youth without histories of STB. In a prospective study, greater decreases in RSA in response to a public speaking task predicted subsequent STB (Giletta et al., 2017); this was not

replicated in a study that used unsolvable puzzles as the physiological challenge (Wieglus et al., 2016). Thus, as seen in adults, lower tonic PNS activity may confer risk for adolescent STB, but unlike the adult literature, either exaggerated (i.e., greater RSA decreases in response to stimuli) or reduced (i.e., smaller RSA decreases) could demark increased risk for youth reporting both concurrent and future suicidality.

There have been fewer studies focused on adolescent STB and SNS activity, as assessed using SCR or pre-ejection period (PEP). Youth with prior histories of STB displayed greater sympathetic reactivity (i.e., increases in SNS) to an unsolvable puzzle than youth with depression and healthy youth (Yang et al., 2019). Adolescents who engaged in non-suicidal self-injury (NSSI), a known risk factor for STB (Cavanagh et al., 2003; Chan et al., 2016; Hawton et al., 2013), evinced increased sympathetic reactivity in response to a mild distress task compared to their peers without histories of NSSI (Nock & Mendes, 2008), although this was not replicated in a small sample of female adolescents (Crowell et al., 2005). Thus, contrary to research with adults, greater SNS reactivity to stressors may characterize youth with, or at risk for, STB, and it is unclear whether baseline SNS activity is associated with STB risk.

Social Exclusion as a Stressor for Adolescents

STB risk is multifactorial (Carballo et al., 2020; Zygo et al., 2019). Interpersonal adversity is a negative experience reliably associated with greater risk for psychopathology in adolescence (Platt et al., 2013), including suicidality (Paul, 2018). Social exclusion specifically, or the experience of being rejected or ostracized by others, is detrimental for adolescent wellbeing (Killen et al., 2008; Killen & Rutland, 2011), can provoke feelings of social stress (Wang et al., 2017), and confers risk for STB (Longobardi et al., 2020). Cyberball is an electronic ball-tossing game in which participants are excluded by two other players, and is an ecologically valid

paradigm demonstrated to induce feelings of rejection in adolescents (Eisenberger et al., 2003; Masten et al., 2009). In two small studies of STB involving PNS responses to Cyberball, greater decreases in RSA during social exclusion trials characterized suicidal youth and their families, compared to non-clinical families (Kaufman et al., 2018), but smaller RSA decreases were noted for college-aged adults reporting suicidal ideation, compared to those without suicidal ideation (Chesin et al., 2020); the latter sample was 42% Latino. Examining stress responses during social exclusion in Mexican-origin adolescents is apt given the unfortunately common experience of racial and ethnic discrimination faced by Latino youth in the U.S. (Benner & Graham, 2011). Similar to other social challenge tasks used in previous STB studies, examining ANS responses to Cyberball in a Mexican-origin adolescent sample could provide evidence for how particular stress responses are related the likelihood of endorsing past or forthcoming suicidality.

Current Study

Mexican-origin and other Latino adolescents are at greater risk for internalizing problems due to exposure to stressors such as ethnic discrimination (Brittian et al., 2013) and acculturative stress (Wu et al., 2020), suggesting it could be particularly important to gain insight into how their stress physiology is related to STB. Considering the rise in suicidality amongst youth in the US, including in the Latino population, measuring autonomic stress activity presents a unique opportunity to further examine whether unique biological markers are associated with past and prospective suicidality.

Given the documented associations between ANS activity and STB, the current study measured both basal and task RSA and SCR in relation to past and subsequent suicidality in a sample of Mexican-origin male and female adolescents. Prior work with this sample showed that, compared to youth who had not reported STB, youth endorsing STB had lower self-control,

greater negative emotionality (Lawson et al., 2021), lower familism and increased family conflict (Gonzalves et al., in press), and that female and U.S.-born adolescents reported more STB than male and Mexican-born (Gonzalves et al., in press). The present work evaluated how Mexican-origin adolescents' basal and acute ANS physiology may reveal autonomic patterns of responding to environmental demands that are associated with (1) prior history of STB and (2) subsequent reports of STB in Mexican-origin adolescents. We tested the following hypotheses:

(1) Mexican-origin youth with a history of STB, compared to those without a history of STB, were expected to evince lower basal RSA

(2) Mexican-origin youth with a history of STB, compared to those without a history of STB, were expected to display greater SCR activation to Cyberball social exclusion.

(3) Lower basal RSA was expected to predict greater likelihood of STB at follow-up.

(4) Greater SCR activation during Cyberball social exclusion was expected to predict greater likelihood of STB at follow-up.

Given the lack of consistent findings in prior research on relations between adolescent STB and both resting state SCR and RSA activation to challenges, we did not advance *a priori* hypotheses about how either ANS measure would be associated with youth STB.

Method

Participants

Participants were 229 Mexican-origin adolescents (M = 17.16 years, SD = 0.44, 110 females) enrolled in a neurobiological sub-study (Guyer et al.) of the larger longitudinal study, the California Families Project (CFP; Robins et al.). Participants in the main study included 674 families with a child in fifth grade (M_{Age} = 10.85 years, 50% female) who were drawn at random from school rosters during the 2006–2007 and 2007–2008 academic years. The sub-study was

designed to examine neurobiological mechanisms in the etiology and development of depression in late adolescence. Thus, youth with elevated but sub-clinical depressive problems were oversampled from the CFP, using counts of adolescents' self-reported symptoms in 9th grade (ages 14–15) based on the Diagnostic Interview Schedule for Children-IV (DISC-IV; Shaffer et al., 2000) and the Anhedonic Depression and General Distress subscales of the Mood and Anxiety Symptom Questionnaire (Clark and Watson, 1995). Scores above the sample median on any of these three measures indicated presence of risk for depression. A dichotomous recruitment variable referring to depression-risk (1 = *scored above the median on any recruitment measure*; *n* = 175, 0 = *scored below the median on all measures*; *n* =54) was controlled for in analyses. No participants met diagnostic criteria for major depressive disorder based on the DISC-IV at the time of sample selection. Parents provided informed consent for their child's participation and youth provided assent. This study was approved by the research site's Institutional Review Board.

Procedure

For data collected as part of the larger CFP study, trained research staff interviewed participants in their homes in either Spanish or English, based on participant preference, annually from ages 10- to 19-years-old. Interviewers were all bilingual and most interviewers were of Mexican heritage.

Participants' neurobiological data were collected when participants were 16- to 17-years-old and between the 7th and 8th year of data collection for the CFP. Participants visited a hospital research facility with one parent and participated in a functional magnetic resonance imaging (fMRI) scan with simultaneous electrocardiogram (ECG) and electrodermal activity (EDA). Over an hour after participants' arrival, baseline ECG and EDA were collected for 3 minutes

while the participants were lying on the scanner bed and outside of the fMRI. Adolescents then completed a structural scan and a set of 3 tasks in the scanner; the second task was the social exclusion challenge, Cyberball (Eisenberger et al., 2003). After receiving instructions, participants played 12 rounds of Cyberball, including six Inclusion and six Exclusion rounds, always presented in the same pseudorandom order. Throughout the Inclusion round, the other players were equally likely to throw the ball to the participant or each other. However, during Exclusion, near the beginning of the round, the other players stopped throwing the ball to the participant and continued throwing it only to each other. Each round lasted 36-seconds, and the total task duration was 7-minutes 23-seconds.

To obtain reports of subsequent reports of STB, participants completed additional questionnaires both as part of the main study and the second part of the sub-study (not reviewed here). Questionnaires were completed over the next 9 to 30 months on four different occasions.

Measures

Suicidal Thoughts and Behaviors

To ensure discretion and given the sensitive nature of the STB questions, youth responded to the measures assessing STB without the help of the interviewers (i.e., youth reported their responses directly on a computer that was turned away from interviewers), apart from the administration of the clinical interview (e.g., DISC or DIS, depending on age).

Lifetime STB. Lifetime STB was captured by utilizing participants' responses to the NIMH Computerized Diagnostic Interview Schedule for Children (CDISC-IV; Shaffer et al., 2000) and a brief suicide questionnaire adapted from the Youth Risk Behavior Survey (Brener et al., 2013) from several previous waves of data collected prior to this study and during the main CFP study. The CDISC-IV is a fully structured diagnostic interview designed for use by non-clinicians to

measure common psychiatric symptoms in children (Shaffer et al., 2000). In the annual assessments when participants were in 5th through 11th grade, youth responded (0 = *no*, 1 = *yes*) to two DISC-IV items assessing STB. The suicide questionnaire was administered annually from 6th through 11th grade and included three items to assess STB in the past 12 months; i.e. "Have you thought about committing suicide?"; "Have you made a plan for committing suicide?"; "Have you attempted suicide?" (1 = *never*, 2 = *once*, 3 = *twice*, 4 = *3 or more times*).

After visits were completed and interviews were examined by research staff, parents were contacted if youth reported having any imminent thoughts of self-harm and/or suicide. Although study questions did not specifically probe for imminent risk, if youth spontaneously reported active suicidality, research staff contacted caregivers and made appropriate referrals.

A dichotomous STB score was derived from the two DISC-IV items in 5th grade plus the three additional items in all subsequent years (i.e., 6th-11th grade). Participants' affirmative responses to one or more of the items were scored as 1 ("yes") for STB at that grade. Participants responding "never" or "no" to all items were scored as 0 ("no") for STB at that grade. The intra-class coefficient for the five items used to generate the final STB score ranged (across individual years) from α = .53 - .78 ($M\alpha$ = .68).

Prospective STB. STB at follow-up were assessed using multiple instruments at 9 months, 18 months, 24 months, and 30 months after completing the ANS measurement. In home visits collected through the larger CFP study, all participants completed the DISC-IV at 9 months (M = 17.55 years, SD = .40) and the adult DIS-IV (Robins et al., 1995) at 30 months (M = 19.73 years, SD = .44); participants also completed the suicide questionnaire at 9, 18 (M = 18.59 years, SD = .40), and 30 months. At 24 months (M =19.05 years, SD = .59), participants returned to the same hospital research facility and completed the Beck's Depression Inventory (BDI; Beck et al.,

1996) and the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock, et al., 2007), each of which included items that assessed STB. The BDI and SITBI measures were obtained for the participants in the second phase of the Neurobiology of Depression sub-study, and supplement the data collected in the larger CFP annual data collection. Participants' affirmative responses to one or more of the items on any of the instruments at any of the timepoints were scored as 1 ("yes") for future STB. Participants responding "never" or "no" to all items on all instruments were scored as 0 ("no") for future STB.

In addition to the STB protocol mentioned above, a clinical psychologist was on-call and available for consultation when participants endorsed STB on the BDI and SITBI measures. Additionally, for youth reporting imminent feelings of wanting to harm or kill themselves, interviewers provided a mental health resource sheet and contracted the participant for safety until the youth could be transported to the nearest emergency department for evaluation. No youth died by suicide (or by any other cause) during the duration of the study.

Physiological Data Processing

RSA

ECG were collected simultaneously with the fMRI scan using three electrodes on the chest connected with Biopac fMRI compatible wireless signal logging (Biopac Systems, USA) through Siemens' telnet MPCU, with a sampling frequency of 400 Hz. Data were converted into an ASCII formatted string of amplitude values that was then fed into Mindware HRV software (Mindware Technologies, Gahanna, OH). The inter-beat-interval sequence was used to calculate RSA. Trained research assistants visually reviewed ECG data for accurate identification of R-spikes and corrected data when the automated program misinterpreted the R-spikes. RSA was calculated in 30-second epochs by Mindware which were then average across the 3-minute

baseline. RSA was then calculated over the duration of each Cyberball exclusion trials and then averaged across the six trails. Inclusion trails were not included in these analyses. RSA data for 10 individuals during baseline and 27 during Cyberball were missing due to human error, equipment errors during sample collection, or high-frequency noise in the ECG signal caused by fMRI interference. All RSA values are expressed in units of log (beats/min^2/Hz).

SCR.

EDA data were obtained before and during the fMRI scan using two electrodes on the palm of the non-dominant hand using Biopac MP150 equipment and AcqKnowledge 4.1 software, with a gain of 10 μS (Biopac Systems, USA). To account for high-frequency noise in the fMRI signal, a rolling filter was applied using Mindware EDA software (Mindware Technologies, Gahanna, OH). For each 30-second segment, the number of nonspecific skin conductance responses (SCR) with an amplitude change of 0.05 μS was counted (Braithwaite et al., 2015). SCR were counted for each 30-second epoch during baseline acquisition, and then averaged across epochs to index baseline SCR. SCR were counted within each Cyberball exclusion trial and then averaged across epochs to index social exclusion task SCR.

Data Analysis

Bivariate associations first were examined with zero-order correlations and *t*-tests. Then, to test whether having a prior history of suicidality would be associated with participants' autonomic stress physiology during baseline (prior to Cyberball) and social exclusion (during Cyberball) at the time of the scan, we utilized two-way (2 x 2) mixed-design analyses of covariance (ANCOVA), with STB history (Lifetime STB endorsement vs. no STB) treated as a between-subjects variable and ANS measurement (baseline vs. task) treated as a within-subjects variable, and controlling for age, sex, depression recruitment status, antidepressant medication

use, and body-mass index (BMI) at the time of the physiology measurement. RSA and SCR were examined in separate ANCOVA models. Parallel ANCOVA models also were examined to test associations between subsequent STB and ANS measures.

Finally, we used path analysis with a binary outcome to examine whether RSA and SCR at baseline and during Cyberball social exclusion made independent contributions to adolescents' likelihood of prospective STB. A dichotomous measure of prospective STB (9-30 months following the ANS measurement) was regressed onto baseline and task scores (modeled as manifest predictors), while covarying age, sex, depression recruitment status, antidepressant medication use, BMI, and lifetime STB reported prior to the ANS assessment. To examine whether the ANS variables accounted for a significant amount of the model variance, we ran three models: covariates only (Model 1); covariates plus baseline RSA and SCR (Model 2); and covariates plus baseline and Cyberball exclusion task RSA and SCR (Model 3).

Missing Data and Outliers

Neither STB variable (i.e., life history or prospective) had missing values. Across the covariates, missing data ranged from 0 to 4.4%. For the ANS (i.e., independent) variables, missing data range from 8.30% to 13%. To account for missing data in the independent variables (ANS variables) and covariates we used full information maximum likelihood (i.e., FIML). To test for potential biases in the missing data, we ran Little's (1988) MCAR's test and the data were determined to be missing completely at random, $\mathcal{X}^2(67) = 62.43$, $p = .64$. Model fit was evaluated using *R*-squared values across path analysis models.

Outliers (i.e., values greater than 3 standard deviations beyond the mean) in the dependent variables were winsorized to bring the values within 3 standard deviations of the mean.

Descriptive statistics and repeated measures ANCOVA analyses were run using *SPSS 28*. The path analysis was implemented using *Mplus 8.0* (Muthén & Muthén, 2018).

Results

Descriptive Statistics

Descriptive statistics and zero-order correlations of key study variables are presented in Table 1. Overall, there was not a significant change in SCR, $t(205) = .45$, $p = .65$, between baseline and Cyberball social exclusion. However, RSA activity significantly decreased from baseline to the social exclusion task across the sample, $t(193) = 10.86$, $p < .001$. Table 2 presents descriptive statistics and *t*-tests comparing baseline and task ANS for youth who did versus did not report lifetime STB, and who did versus did not report STB across the four follow-up assessments (i.e., prospective STB). At Time 1, over 27% of the sample ($n = 62$) had endorsed STB at least once since their 5th grade year and nearly 20% of the sample ($n = 45$) went on to endorse suicidality at least once during follow-up (i.e., 6-30 months following Time 1), with 60% ($n = 27$) of those participants having also endorsed lifetime STB. Participants who reported histories of STB had significantly lower baseline SCR than youth without lifetime STB. Youth who reported subsequent STB at follow-up evinced significantly lower baseline SCR and significantly higher RSA during the social exclusion task, compared to their peers who did not evince prospective STB (see Table 2).

Lifetime STB predicting autonomic physiology

SCR. The ANCOVA for SCR revealed a significant main effect for lifetime STB, $F(1,192) = 6.56$, $p < .05$, partial $\eta^2 = .03$. Participants with a history of endorsing STB prior to the scan had overall lower SCR across baseline and task ($M = 1.87$, $SD = 1.65$) (i.e., hypoactivation) during Cyberball social exclusion, compared to participants without a history of STB

Table 3.1 Descriptive Statistics and Zero-order Correlations of Key Study Variables

Key Variable	*M (SD)*	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. Age	17.16 (.43)	--										
2. Sex	--	.01	--									
3. BMI	25.35 (5.65)	.04	**-.17****	--								
4. Depression	.76 (.43)	-.12†	**.16***	-.01	--							
5. Medication	.12 (.33)	-.01	**.14***	.05	.12†	--						
6. Lifetime STB	.27 (.46)	-.04	**.24****	.02	**.18****	.10	--					
7. Prospective STB	.20 (.40)	-.08	**.19****	-.02	.12†	**.18****	**.37****	--				
8. Baseline RSA	6.82 (.98)	.04	**.20****	**-.23****	.01	.03	.06	-.04	--			
9. Task RSA	6.17 (1.11)	.04	**.14***	**-.26****	.04	.03	.05	.14†	**.67****	--		
10. Baseline SCR	2.45 (2.25)	.01	**-.16***	**.14***	-.13†	-.05	**-.18****	**-.21****	.13†	.05	--	
11. Task SCR	2.44 (1.91)	.01	**-.17***	.14†	-.05	.01	-.12†	.13†	-.08	.01	**.20****	--

Note. BMI = Body Mass Index, STB = suicidal thoughts and behaviors, RSA = respiratory sinus arrhythmia, SCR = skin conductance response. Sex was coded as 1 = *female*, 0 = *male*. Medication use was coded dichotomously, 0 = *no*, 1= *yes*. All physiological measures were recorded when participants came to the lab for the fMRI scan. Both lifetime and prospective STB were scored dichotomously, *yes* = 1, *no* = 0. Significant correlations are in bold and denoted as †$p < .10$, *$p < .05$, **$p < .01$.

Table 3.2 Means, Standard Deviations, and T-tests of ANS Variables by Lifetime and Prospective STB groups

	Lifetime STB				Prospective STB			
	Yes	No	T-test		Yes	No	T-test	
	M(SD)	*M(SD)*	*t(df)*	*p*	*M(SD)*	*M(SD)*	*t(df)*	*p*
Baseline SCR	**1.77(.146)**	**2.69(2.43)**	**2.70(216)**	**< .01****	**1.52(1.41)**	**2.68(2.36)**	**3.09(216)**	**< .001*****
Task SCR	2.10(1.92)	2.58(1.89)	1.69(208)	.09†	2.92(2.11)	2.31(1.84)	-1.87(208)	.06†
Baseline RSA	6.91(.99)	6.79(.98)	-.82(213)	.41	6.74(.86)	6.84(1.01)	.61(213)	.54
Task RSA	6.26(1.03)	6.14(1.13)	-.68(195)	.49	**6.48(.90)**	**6.10(1.14)**	**-1.96(195)**	**< .05***

Note. ANS = autonomic nervous system, RSA = respiratory sinus arrhythmia, SCR = skin conductance response, STB = suicidal thoughts and behaviors. Task refers to the Cyberball social exclusion trials. All physiological measures were recorded when participants came to the lab for the fMRI scan. Both lifetime and prospective STB were scored dichotomously, *yes* = 1, *no* = 0. Significant correlations are in bold and denoted as †$p < .10$, *$p < .05$, **$p < .01$, ***$p < .001$.

(M = 2.68, SD = 2.15). There also was a main effect of sex, $F(1,192) = 4.64$, $p < .05$, partial η^2= .02, with male participants showing greater sympathetic arousal (M = 2.78, SD = 1.63) compared to female participants (M = 2.11, SD =1.51).

RSA. Contrary to predictions, there was no significant main or interaction effects in the model for baseline RSA and lifetime STB. Similarly, there were no effects for RSA activation and lifetime STB.

Autonomic physiology predicting subsequent STB

SCR. The ANCOVA for SCR revealed a significant measurement by prospective STB interaction, $F(1,192) = 14.27$, $p < .001$, partial $\eta^2 = .07$. In support of predictions, participants who prospectively endorsed STB at follow up evinced a significant increase in SCR from baseline (M = 1.59, SD = 1.41) to social exclusion task (M = 2.88, SD = 2.11), $t(40) = -3.32$, $p < .01$. Conversely, adolescents who did not endorse subsequent STB at follow-up showed a significant decrease in SCR from baseline (M = 2.71, SD = 2.37) to social exclusion task (M = 2.28, SD = 1.81), $t(164) = 2.13$, $p < .05$.

RSA. The ANCOVA for RSA revealed a significant measurement by prospective STB interaction, $F(1,180) = 9.70$, $p < .01$, partial $\eta^2 = .05$. Adolescents who prospectively endorsed STB at follow up evinced a significant but small decrease in RSA from baseline (M = 6.74, SD = .88) to social exclusion task (M = 6.46, SD = .90), $t(37) = 2.40$, $p < .05$, whereas adolescents who did not endorse subsequent STB at follow-up showed a significant and larger decrease in RSA from baseline (M = 6.85, SD = 1.01) to social exclusion task (M =6.09, SD = 1.14), $t(155) = 11.05$, $p < .001$.

Path Analysis. Next, we implemented a SEM (i.e., path analysis) with a binary outcome to examine whether autonomic physiology was predictive of prospective STB 9-30 months

following the initial laboratory visit (see Table 3). We ran three different models in a stepwise fashion to examine covariates alone (Model 1), covariates with baseline ANS variables (Model 2), and covariates with baseline and task ANS variables (Model 3). Model 1 produced a $R^2 = .23$; adding baseline ANS measures accounted for another .09, to $R^2 = .32$; and finally adding social exclusion ANS variables accounted for another .13, to $R^2 = .45$.

For Models 1-3, having a prior history of STB increased the odds of subsequently reporting suicidality over and above all other covariates. Once the resting state ANS variables were included (Model 2), participants who evinced lower baseline SCR were more likely to endorse subsequent STB (i.e., for every unit decrease in baseline SCR, participants had 32% greater odds of reporting STB at follow-up). Once the social exclusion task ANS variables were included (Model 3), resting state RSA also showed a significant relation to subsequent STB, such that for every unit decrease in baseline RSA participants had more than twice the odds ($1/OR = 2.04$) of endorsing subsequent STB. However, given that baseline RSA became significant only following the inclusion of the ANS task variables, its contribution to increased odds of subsequent STB should be interpreted within the context of parasympathetic activity to the exclusion trials.

Regarding participants' ANS scores during the social exclusion task, relatively higher SCR and RSA were significantly related to an increased likelihood of reporting STB at follow-up. Noting that, on average, Cyberball exclusion elicited PNS withdrawal without SNS activation, this suggests that participants who displayed larger increases in SNS activity and smaller decreases in PNS activity during social exclusion trials were at greater risk for prospectively suicidality 9- to 30-months later in partial support of predictions. Specifically, higher SCR during social exclusion was related to a 37% increase in odds of subsequent STB

Table 3.3 Predictive Associations Between Covariates, Autonomic Physiology Scores, and Prospective STB 9-30 Months Following the Scan: Results of Path Analyses

	Model 1 $R^2 = .23^{**}$		Model 2 $R^2 = .32^{***}$		Model 3 $R^2 = .45^{***}$	
Variable	*B*(SE)	*OR* (95% CI)	*B*(SE)	*OR* (95% CI)	*B*(SE)	*OR* (95% CI)
Age	-.40 (.38)	.67 (.32 - 1.41)	-.47 (.46)	.63 (.30 - 1.36)	-.62 (.52)	.54 (.23 - 1.26)
Sex	.53 (.19)	1.69 (.88 - 3.25)	.52 (.41)	1.69 (.86 - 3.33)	.68 (.44)	1.98 (.95 - 1.09)
BMI	-.01 (.87)	1.00 (.94 - 1.05)	-.003 (.04)	1.00 (.94 - 1.06)	.01 (.04)	1.01 (.95 - 1.08)
Depression Symptoms	.23 (.65)	1.26 (.55 - 2.91)	.15 (.52)	1.16 (.49 - 2.71)	.20 (.57)	1.23 (.48 - 3.12)
Medication Use	.92† (.06)	2.51 (1.12 - 5.61)	.95† (.51)	2.58 (1.13 - 5.93)	**1.04* (.53)**	**2.84 (1.19 - 6.78)**
Lifetime STB	**1.66** (.38)**	**5.23 (2.81 - 9.76)**	**1.60*** (.39)**	**4.94 (2.61 - 9.33)**	**1.90*** (.44)**	**6.67 (3.23 - 13.78)**
Baseline RSA	--	--	-.16 (.21)	.85 (.60 - 1.21)	**-.72* (.33)**	**.49 (.28 - .84)**
Baseline SCR	--	--	**-.28* (.12)**	**.76 (.62 - .93)**	**-.28* (.13)**	**.76 (.62 - .94)**
CB Exclusion RSA	--	--	--	--	**.86** (.32)**	**2.36 (1.40 - 3.98)**
CB Exclusion SCR	--	--	--	--	**.32** (.11)**	**1.37 (1.14 - 1.65)**

Note. STB = suicidal thoughts and behaviors, RSA = respiratory sinus arrhythmia, SCR = skin conductance response, BMI = Body Mass Index. Sex was scored *female* = 1, *male* = 0. Both scores of STB were scored as a dichotomously *yes* = 1, *no* = 0. BMI, Age, and ANS variables were measured at the same timepoint. Significant estimates are in bold and denoted as $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

and higher task RSA (less withdrawal) during social exclusion was predictive of more than a twofold increase in odds of subsequent STB. Although youth who both did and did not report STB at follow-up evinced RSA withdrawal during social exclusion, those who went on to report STB evinced significantly less withdrawal than their peers who did not (see Table 2), suggesting less parasympathetic flexibility (Porges, 2007).

Discussion

The goal of this study was to test whether lifetime or prospective STB was related to baseline autonomic activity as well as PNS and SNS stress responses to a social exclusion challenge in a sample of Mexican-origin youth with modest depression problems. The present work is the first longitudinal study to examine autonomic physiological responses to acute stress as it relates to suicidality in an exclusively Mexican-origin sample of adolescents. Our demonstration that sympathetic hypoactivation was related to endorsing a lifetime history of STB in Mexican-origin adolescents is a novel replication of prior findings with adult samples in the adolescent literature. Additionally, our study is the first to prospectively show that autonomic tonic hypoactivity and sympathetic dominance (i.e., higher SNS activity paired with minimal RSA withdrawal) in response to social exclusion predict greater likelihood of subsequent STB in adolescents. Not only does this work provide further evidence for potential biomarkers of suicidality risk, but it also extends prior research to include adolescents and emerging adults of Mexican origin.

Lifetime STB. Our first set of analyses examined whether participants with a history of STB displayed a unique physiological profile compared to their peers without prior STB. We found that overall SCR, but not RSA, was significantly lower in youth with histories of STB. This work is the first adolescent study to provide evidence for SNS hypoactivity as a possible biomarker for STB. Prior research with depressed and suicidal adults reveals a similar pattern of lower

sympathetic activity compared to healthy individuals (Bonnet et al., 2004; Thorell, 2009; Thorell et al., 2013; Wolfersdorf et al., 1996). The limited studies with adolescents have produced mixed findings, with research showing no differences in sympathetic activity between parasuicidal youth and controls (Crowell et al., 2005), and other work revealing greater SNS activation in response to a stressful task (Nock & Mendes, 2008), but no baseline differences between groups (Yang et al., 2019). Given the variability of methods used to induce stress or emulate a challenge, these studies may be tapping into different types of stress responses that may or may not be related to suicidality. Additionally, Crowell et al., who also measured EDA, used a sample of only 23 adolescent females with histories of NSSI, opposed to thoughts and behaviors with suicidal intent, suggesting that characteristics of the study participants and low statistical power may have led to their lack of SCR findings.

The adult literature has produced more consistent results showing that low electrodermal (i.e., SNS) activity is a reliable marker of depression, and more specifically, suicide risk. Our study revealed an association between suicidality and SCR hypoactivation, over and above depression severity, suggesting that youth with past STB possess distinctive sympathetic profiles or even physiological scars (Yang et al., 2019), compared to adolescents who do not share this history. As posited by prior research, sympathetic under-arousal may be associated with low behavioral inhibition (Beauchaine, 2001; El-Sheikh et al., 2009), or diminished ability to increase vigilance and attention to facilitate risk assessment and curb impulsive behaviors which may involve negative consequences (McNaughton & Corr, 2004). Impulsivity is one of the most researched cognitive processes associated with youth suicidality (Cha et al., 2018), and has shown associations with suicidal ideation and behaviors (Kasen et al., 2011; McKeown et al., 1998). Additionally, SNS hypoactivity has also been linked with the emergence of externalizing

behavior (Cappadocia et al., 2009), which has been theorized to reflect a lower sensitivity to threat or an increased need to engage in disruptive behavior, perhaps to extinguish the unpleasant feelings associated with low sympathetic arousal (Cappadocia et al., 2009; Raine et al., 1997). Considering that fight-or-flight aspects of SNS activity (i.e., increased sympathetic arousal) can be behaviorally inhibitory and protective from perceived or real threat (Obradović & Boyce, 2012), a weaker inhibitory signal in the context of acute stress may contribute to engagement in suicidal thoughts or actions. Youth who cannot effectively cope with their external environment or who have become psychologically or behaviorally uninhibited in response to social challenges may also be at heightened risk of suicidality as their ability to adequately assess harm and threat is reduced.

In contrast to previous research revealing support for associations between RSA and lifetime STB, we did not observe a significant parasympathetic difference in our sample. That is, youth with and without histories of STB did not differ across parasympathetic activity (i.e., baseline and task). However, similar to work measuring SCR, much of the adolescent RSA research has utilized different methodologies to induce stress, including the use of both cognitive and social tasks, which may explain the variability in RSA findings (Obradović et al., 2011). Further, adolescents were included in the lifetime STB group if they had endorsed at least once in the previous seven years, so it is possible that the association between suicidality and RSA may be temporal. Importantly, adult samples often represent a higher level of STB severity (including individuals who eventually die by suicide) whereas adolescent samples predominantly include those who have contemplated suicide but often not made any attempts. Variability in clinical acuity may explain differences in sympathetic activity between adult and adolescent samples, but additional research is needed to resolve discrepancies.

Prospective STB. To examine associations between participants' ANS physiology and prospective STB, we first modeled resting state RSA and SCR as predictors without the task physiological variables. Participants who displayed lower tonic (baseline) sympathetic and parasympathetic activity were more likely to endorse suicidality 9- to 30-months later. Thus, the hypothesized effect of basal RSA was specific to prospective STB risk. Similar to our finding for lifetime STB, low basal SCR also predicted prospective STB risk; this was a novel finding in studies of adolescent STB and reveals an earlier emergence of SNS hypoactivity as a biomarker for STB risk that previously has been shown only in adults (Sarchiapone et al., 2018; Thorell, 2009).

It is important to note that baseline RSA did not significantly predict subsequent STB until task ANS variables were included in the model. Low baseline RSA is a well-established biomarker for poor emotion regulation (Beauchaine, 2015; Beauchaine & Thayer, 2015) and this work is the first to demonstrate that it predicts forthcoming adolescent suicidality. However, the contribution of tonic PNS activity to prospective STB must be interpreted within the context of PNS activity in the exclusion task. Parasympathetic withdrawal to a social challenge also has been associated with better emotion regulation (Hastings & Kahle, 2019). Hence, those Mexican-origin youth who exhibited lower tonic RSA followed by a less dynamic parasympathetic response to Cyberball social exclusion may have had a parasympathetic profile that conferred greater propensity for adjustment difficulties (Smith et al., 2020), psychopathology (Beauchaine & Thayer, 2015), and suicidality.

Further considering the social exclusion task ANS measures, adolescents who endorsed subsequent STB displayed an elevated SCR response paired with minimal RSA withdrawal in reaction to Cyberball exclusion, and thus revealed evidence of greater stress activation without

allocation of vagally mediated regulation resources (Porges, 1992, 2007). As predicted, Mexican-origin youth who later endorsed STB manifested a pattern of sympathetic activation indicating they found the social exclusion task threatening (Mestanik et al., 2014), extending prior cross-sectional evidence that youth from other communities who endorse STB evince stronger SNS reactivity (Nock & Mendes, 2008). Individuals with attenuated parasympathetic responses (e.g., blunted RSA withdrawal) may lack the flexible and self-regulatory capacity to adapt rapidly to stressors (Porges, 1992), and Mexican-origin youth who subsequently reported STB displayed a mild RSA increase in response to being social excluded, mirroring findings that both adolescents and children with histories of STB display reduced parasympathetic reactivity (James et al., 2017; Yang et al., 2019).Considered in whole, the path analysis revealed that low tonic dual-branch autonomic activity followed by increased phasic SNS activity without reciprocal PNS withdrawal increased adolescents' odds of endorsing STB over the next 30 months. Yang and colleagues (2019) found a similar dual-branch ANS reactivity in youth with histories of STB; our extension of this work suggests that weak PNS responses paired with strong SNS responses may be a multisystem biomarker for prospective STB risk in adolescence. Youth who fail to mobilize adaptive parasympathetic modulation, and sympathetically respond to moderate challenges as potential threats, may become behaviorally and emotionally dysregulated easily, exacerbating their risk for suicidality, and possibly other psychopathology. Conversely, adolescents who did not report any subsequent suicidality did not show evidence of a fight-or-flight response, but rather evinced a modest and significant decrease in SCR from baseline to Cyberball exclusion with a simultaneous decrease in RSA, suggesting an adaptive orientation and engagement response (Porges, 2007).

Considering that adolescence is a period of rapid physiological and psychosocial changes (Prinstein & Miller, 2019), maladaptive responses to social exclusion, a common experience during this developmental period (Romano et al., 2011), may signal a vulnerability for stress dysregulation. Our sample was exclusively Mexican-origin and may be more likely to endure negative experiences related to social exclusion, such as ethnic discrimination or acculturative conflict, compared to their non-Latino peers (Hovey & King, 1996; Perez et al., 2008). Future research could utilize moderation analyses to help reveal whether certain negative, and culturally specific experiences, interact with stress physiology and lead some youth to develop STB in adolescence.

Although this study had many strengths, there are some important limitations to note. First, the adolescents who participated in this study were exclusively Mexican-origin, making this research the first of its kind, but it is important not to generalize these findings to adolescents of other Latino backgrounds, given the heterogeneity of different cultures and practices within the broader U.S Latino communities (Roth et al., 2019). Second, when measuring both lifetime and prospective STB, our analysis allowed for endorsements that were both years old and years in the future, respectively. Forthcoming work should strive to identify more proximal risk factors associated with imminent STB, as most adolescent research has focused on distal predictors which are often transdiagnostic and not specific to suicidality (Cha et al., 2018; Miller & Prinstein, 2019).

In conclusion, adolescence represents a developmental period of heightened risk for interpersonal stress (McLaughlin & Nolen-Hoeksema, 2012; Parker et al., 1995), physiological dysregulation (Crowell et al., 2014) and suicidality (Miller & Prinstein, 2019). There is limited research studying possible biomarkers for increased suicide risk in youth and studies examining

the links between psychophysiology and STB in Latino youth are nonexistent prior to this current work. Among the current research, the adolescents who failed to adaptively respond to their environments, whether through a lack of baseline autonomic arousal or a disproportionate stress response, appeared to be the most vulnerable for STB. Future research should continue to investigate the interplay between the sympathetic and parasympathetic acute stress responses rather than examining each branch in isolation. Failing to account for activity across the complete autonomic stress system offers only partial answers in the search for reliable biomarkers of youth suicidality.

Despite the growing concern with the prevalence of adolescent suicidality, researchers' ability to predict suicidal ideation and behavior, including completed suicides, remains remarkably inadequate (Franklin et al. 2017). Understanding and identifying the autonomic correlates of youth suicidality provides generative avenues for objective and early identification of developing STB. The constellation of high suicidal risk implicates several factors across social, cultural, and neurobiological contexts (Miller & Prinstein, 2019), and utilizing physiological indices of risk may advance the efforts toward prevention and early intervention.

CHAPTER FOUR

STUDY 3: PARASYMPATHETIC AND PUBERTAL CORRELATES OF LIFETIME AND PROSPECTIVE SUICIDAL THOUGHTS AND BEHAVIORS IN CLINICALLY HIGH-RISK FEMALE ADOLESCENTS

Background

Prevalence rates of suicidal thoughts and behaviors (STB) in adolescence continue to rise in the U.S. (Twenge, 2020) and this is especially true for adolescent females (Ivey-Stephenson et al., 2020). For all youth aged 10-14, deaths due to suicide increased threefold from 2007-2017 (Curtin & Heron, 2019). And most recently, from 2019 to 2021, the mean weekly number of emergency room visits for suicide attempts among females aged 12-17 increased by more than 50%, largely due to the far-reaching consequences unique to school-aged youth during the global COVID-19 pandemic (Yard et al., 2021). For adolescents, the pubertal transition is a period of immense social, neurological, and physiological change (Juraska & Willing, 2017; Spear, 2003) and has emerged as a correlate of physiological and psychological risk for psychopathology, including depression (Ge et al., 2001). The start of puberty foments a neurobiological process that influences the maturation of the neural circuitry that guides emotion regulation and impulsivity (Ho et al., 2022), two socioemotional facets related to adolescent STB (Hatkevich et al., 2019). Additionally, early pubertal timing in females, or when a child enters puberty earlier compared to her same-aged peers, has been associated with negative psychological outcomes (Mendle et al., 2007), including heightened risk for suicidality (Wichstrøm, 2000). The hormonal shifts of puberty (Sizonenko, 1978), and elevated physiological sensitivity to stressors in adolescence (Stroud et al., 2009), may together result in a heightened vulnerability for acute stress dysregulation (Miller & Prinstein, 2019). Relatedly, there is reliable evidence of

associations between autonomic stress activity and youth STB (Crowell et al., 2005; Giletta et al., 2017; Yang et al., 2019). What remains unknown in the current literature, and the aim of the present study, is whether pubertal timing, a key feature of individual differences in adolescent development, moderates the relation between parasympathetic stress physiology and suicidality in early adolescent females, concurrently or prospectively.

Although we still lack a full understanding of why some adolescent females engage in STB while others do not, contemporary theories of suicidality highlight the importance and interacting forces of emotional dysregulation, biological and physiological systems, and environmental stressors (Linehan, 1993; Miller & Prinstein, 2019). Linehan (1993) proposed that suicidal individuals are hypersensitive to criticizing and invalidating environments, and in their enduring of intense and prolonged negative affective experiences, suicide becomes the ultimate way to extinguish negative affect (Selby, Joiner, & Ribeiro, 2014). A more recent and developmentally informed theory posits that adolescent STB is a "failure of the biological response system" (Miller & Prinstein, 2019, p. 439) to acute stress, and adolescents who manifest other known risk factors (e.g., prior histories of STB, childhood adversity) may engage in suicidality if confronted with stress beyond their individual threshold. Not only is STB viewed as the result of a confluence of multiple risk factors, it is also a highly individualized response, as some youth lack adequate resources to cope with certain challenges while others are able to tolerate the same stressors without resulting in STB. Below, we review biological risk factors (i.e., biological sex, pubertal timing) as well as discuss the adolescent research examining how autonomic physiology has revealed specific patterns unique to individuals who engage in STB.

Biological Sex

Across decades of research, rates of completed suicides for adolescent females are lower than those for adolescent males in several Western countries (Miranda-Mendizabal et al., 2019), but suicidal ideation and attempts follow an opposite trend (Fergusson et al., 2000; Grunbaum et al., 2004). Although fewer females than males die by suicide (as males typically make more lethal suicide attempts), females are consistently more likely to engage in suicidal ideation and planning (Beautrais, 2002; Nock et al., 2013). For example, in a sample of over 5,000 typically developing adolescents, nearly 20% of the girls surveyed retrospectively reported experiencing suicidal ideation, compared to 10% of male youth (Kaess et al., 2011).

Compared to community samples, STB rates are significantly higher in female samples in which the participants also report symptoms of internalizing disorders (e.g., depression and anxiety; D'Eramo et al., 2004), and/or self-harm (Duarte et al., 2020; Mars et al., 2019). For example, in a longitudinal study of clinically high-risk adolescents, females compared to males reported more suicide attempts and non-suicidal self-injury (NSSI) at baseline, evinced greater severity of depression and anxiety overall, and disclosed more suicidal ideation at several prospective timepoints (Prinstein et al., 2008). The gender difference in adolescent suicidality is well established yet the biological mechanisms driving this disproportionality are not well understood. Pubertal timing might prove a generative area to probe.

Pubertal Transition and Timing

Although typical pubertal development alone is not theorized to confer a unique risk for increased suicidality, the transition into adolescence is a period of marked social, affective, and physiological hypersensitivity (Ahmed et al., 2015; Gunnar et al., 2009; K. Rubin et al., 2008; Stroud et al., 2009). The onset of puberty initiates a myriad of changes influencing physical

growth, sexual maturation, emotion regulation, and the potential development of psychopathology (Dahl & Gunnar, 2009; Gunnar et al., 2009; Spear, 2009). Past evidence implies that puberty is associated with a reorganization of the body's stress-response systems, as well as a period of heightened stress and socioemotional reactivity (Dahl & Gunnar, 2009; Miller & Prinstein, 2019). Typical age- and puberty-related increases in cortisol and autonomic responses have been observed in adolescents in response to lab-based performance tasks (Gunnar et al., 2009; Stroud et al., 2009), and this amplified sensitivity to stressors is considered adaptive for most youth, but may be maladaptive for individuals already at risk for psychopathology (Spear, 2009). Spear (2009) theorized that youth undergo normative changes in the neurobiology of stress reactivity across the pubertal transition, including a heightened sensitivity to stressors, which might precipitate the onset of mental health challenges for vulnerable individuals who lack adequate coping resources. Moreover, adolescent females have been identified as being especially at risk for developing psychopathology, such as STB, during this transition (Boeninger et al., 2010; Ge et al., 2001), however the underlying cause is not well understood.

One explanation for the heightened risk for mental health problems observed in females is that the onset of puberty demarcates social changes as well as biological ones. Puberty often accompanies academic transitions in which many adolescents are starting middle or high school and the importance of peer relationships, including romantic ones, become prioritized (Natsuaki et al., 2009). Given the peer-centered environment in which many adolescents exist, and the premium peers can place on group conformity (Rubin et al., 2006), there can be social consequences that accompany atypical pubertal maturation. For example, girls who experience early pubertal timing may be treated differently by peers, receive unwanted attention from males,

and have a greater likelihood of becoming a victim of intimate partner violence during adolescence (Foster et al., 2004).

Furthermore, perceived early pubertal timing (compared to same-age peers) in adolescent females, but not males, has been found to be prospectively linked with increased risk for suicidal behaviors (Wichstrøm, 2000), yet this area of research is sparce. Other studies have found that pubertal status predicted sex differences in depression (D'Eramo et al., 2004), after controlling for age (Angold et al., 1998; Conley & Rudolph, 2009), and internalizing symptoms in general (Hayward et al., 1997), suggesting that pubertal timing may be especially important for psychosocial adjustment. On average, girls enter puberty before boys (Hayward, 2003), which may contribute to the earlier emergence and rise of suicidality in pre- and early adolescent girls.

To date, there are no studies which test whether pubertal timing moderates the association between autonomic stress physiology and psychopathology, including suicidality. Although there is sparse research examining how puberty interacts with neurobiology to predict risk for mental health symptoms in youth, evidence shows that precocious maturation is associated with heightened stress sensitivity to environmental demands (Stroud et al., 2009) and a host of negative psychological outcomes (Mendle et al., 2007). An elevated sensitivity to context (Boyce & Ellis, 2005), paired with an immature stress response system ill-equipped to manage particular stressors, may predispose certain youth to a greater vulnerability for developing psychopathology. To our knowledge, pubertal timing has not been examined as a moderator of the ANS predicting internalizing symptoms or related problems, however, a small set of papers have studied the interaction of the adolescent hypothalamic-pituitary-adrenal axis and pubertal status as it relates to psychopathology. To illustrate, in a sample of previously healthy 9- to 15-year-old girls, early pubertal development moderated the association between cortisol

hypoactivity and the onset of clinical depression (Colich et al., 2015). However, not all research has found a moderating effect but rather revealed a direct pathway. For example, adolescent girls' elevated cortisol stress reactivity in response to an interpersonal stressor mediated the association between early pubertal timing and symptoms of depression and anxiety (Natsuaki et al., 2009). Both studies suggest that the link between an individual's stress response and later psychopathology may depend on the timing of her pubertal development. The well documented association between emotion dysregulation and the PNS, and the heightened stressor sensitivity that accompanies puberty, suggests that girls who evince early pubertal timing may display differential stress reactivity due to a heightened sensitivity to their environment, which may then be related to their risk for STB.

ANS and Adolescent STB

Examining autonomic stress physiology provides an opportunity to investigate potential biomarkers for emotion regulation and dysregulation in relation to developmental psychopathology, including STB. The parasympathetic nervous system (PNS) primarily lowers arousal, acting to downregulate states of high excitement, and promotes restoration and recuperation (Porges, 2007). The PNS traditionally has been referred to as the "rest and digest" branch of autonomic activity (Berntson et al., 2017) and heightened PNS activity is related to emotion states such as contentment and sadness, and physiological changes such as decreased heart rate and pupillary dilation (Hastings & Kahle, 2019). However, the PNS does not only support restorative functioning.

Polyvagal Theory (1995) conceptualized the PNS as a crucial mechanism of the social engagement system (Porges & Furman, 2011), providing a framework to connect anatomical and physiological circuits critical for the body's internal regulation with interpersonal interactions

(Porges & Lewis, 2010). Within this context, heart rate variability (HRV), which corresponds with respiratory sinus arrythmia (RSA), serves as an index of individual differences in physiological contributors to emotional regulation and arousal (Beauchaine, 2001). RSA represents the fluctuation of the heart rate across the respiratory cycle (Beauchaine, 2015; Porges, 2003) and RSA reactivity is a measure of how greatly the PNS modulates its activity (i.e., withdraws or decreases) when responding to the outside environment. Porges (2003) coined the term *neuroception* to describe how changes in RSA in response to a stimulus can uncover an individual's implicit evaluation of its relative safety or social significance.

Previous research has suggested that higher baseline RSA and moderate withdrawal of parasympathetic influence (in response to an aversive stressor) are associated with greater emotion regulation (Beauchaine, 2015; Hastings et al., 2014; Miller & Prinstein, 2019). Evincing responsive and flexible RSA activity across different environments (i.e., both safe and potentially threatening) is crucial for adaptive physiological self-regulation (Hastings et al., 2014). Within the study of adolescent STB specifically, an individual's capacity to adaptively regulate in the face of stressors is crucial for successful social functioning. Considering that poor emotion regulation is reliably associated with both suicidal ideation and attempts in adolescents (Colmenero-Navarrete et al., 2021), and emotion regulation is intimately tied to autonomic stress responsivity, expanding our understanding of parasympathetic stress activation within high-risk adolescents could provide avenues for early STB intervention.

To date, research investigating the associations between parasympathetic physiology and adolescent suicidality has been mixed. Studies that have examined PNS activity as an autonomic correlate of suicide risk reveal that lower resting state RSA and excessive RSA withdrawal (i.e., decreases in RSA) are associated with concurrent and prospective suicidality (Crowell et al.,

2005; Giletta et al., 2017; Miller & Prinstein, 2019). For example, in a small clinical sample of adolescent girls lower baseline RSA and greater RSA withdrawal in response to a sad film clip were associated with endorsing a history of STB (Crowell et al., 2005). Within a larger sample of clinically high-risk female adolescents, greater RSA withdrawal in response to a speech task, but not baseline RSA, was predictive of an increased risk for suicidal ideation 9-months later (Giletta et al., 2017). In an unpublished study of Mexican-origin male and female adolescents, prospective STB was associated with lower baseline RSA, but only when followed by mild RSA augmentation (i.e., increase in RSA) during a social exclusion task, suggesting these participants failed to appropriately modulate their stress response (Gonzalves et al., in preparation).

Other work has observed associations between mild increases in RSA in response to an unsolvable puzzle (Yang et al., 2019) or a challenging conversation with a caregiver (James et al., 2017) and STB, yet there were no differences in RSA withdrawal between youth with STB and controls in either study. Mild RSA augmentation, opposed to moderate RSA withdrawal, in response to a stressor has been interpreted as a blunted or inflexible parasympathetic response (Yang et al., 2019), indicating an individual's failure to respond adaptively to the present environment. Dysregulated parasympathetic stress activation may be indicative of poor emotion regulation, resulting in a greater likelihood of engaging in STB (Linehan, 1993). Managing affective responses across a myriad of situations, as well the ability to cope with day-to-day stressors, are both vital for the psychological wellbeing of adolescents (Daniel et al., 2020).

Current Study

The field of autonomic physiology and adolescent suicidality is relatively nascent and additional research is necessary to understand the links between acute stress neurobiology and risk for STB. Less is understood about how pubertal timing may influence the associations

between the PNS and suicidality in either community or clinical samples. We examined baseline RSA and RSA activation in response to a stressful speech task in an ethnically diverse sample of clinically high-risk female adolescents with histories of depression and/or STB. The present work had two primary goals: (1) examine the associations between adolescent RSA and current and prospective STB; and (2) test whether pubertal timing moderates the associations between adolescent RSA and current and prospective STB. Given the current literature and theory, we advanced the following hypotheses:

(1) Participants who have a lifetime history of STB will evince lower basal RSA compared to their peers with no history of STB.

(2) Lower, compared to higher, basal RSA will be associated with a greater likelihood of prospective STB at follow-up (12 months later), after accounting for participants' history of STB.

(3) Earlier, compared to later, pubertal timing will be positively associated with both lifetime and prospective STB.

(4) The association between low basal RSA and STB will be moderated by pubertal timing: Participants with low basal RSA and early pubertal timing will be more likely to endorse lifetime history and prospective STB compared to their peers with higher basal RSA and later pubertal timing.

Considering the lack of consistent findings for RSA activation and STB, we did not advance any *a priori* hypotheses about the directionality of RSA activation in response to the speech task and its association with either lifetime or prospective STB.

Method

Multiple assessments occurring over a one year in a longitudinal study were conducted to obtain extensive data on suicidal ideation, plans, and attempts over time. At the initial lab visit, biological data were collected to measure autonomic nervous system functioning and reactivity (e.g., RSA) as well as pubertal maturation (i.e., status and timing). The data were collected through a laboratory at the University of North Carolina (Prinstein et al.) and physiological (e.g., HRV) data were processed by the Center for Mind and Brain at the University of California, Davis (Hastings et al.).

Participants

Participants included 229 biological girls ages 9-15 years (M_{Age} = 11.80 years, *SD* = 1.8 years*;* 49.6% Euro-American/Caucasian, 27.4% African American, 12.6% Mixed race or ethnicity, 7.4% Latinx, 1.3% Asian American, 1.3% Native American, < 1% unknown) referred through inpatient or outpatient mental health clinics. Combined or dual gross annual income was recorded at the initial visit and varied greatly across families (*M* = $87,637, *SD* = $82,044). Participants were recruited from a variety of community and clinical placements, including inpatient psychiatric units, outpatient mental health agencies, high schools, and the local community using flyers and mass-email advertisements. Participants recruited from inpatient facilities were not enrolled until two months following discharge from the psychiatric unit. Inclusion criteria were a history of mental health concerns, including mood, anxiety, substance use, or disruptive behavior disorders in the past two years. Exclusion criteria were active psychosis, intellectual disability disorder, or any other developmental disorder. Parents and participants provided written informed consent and assent, respectively, and all procedures were approved by the University of North Carolina's Institutional Review Board.

Procedure

At baseline, participants were at pre-, peri-, and post-pubertal stages of development. Baseline physiological data were collected at the start of the longitudinal protocol, and STB data were collected concurrently and at 4, 8 and 12 months subsequently. At the time of recruitment, all participants either had a history of clinical major depressive disorder or had experienced severe adversity (e.g., poverty, maltreatment), and were exhibiting sub-clinical depressive symptoms.

During the laboratory visit, participants completed several different tasks in the following order: (a) a structured clinical interview to assess prior self-injurious thoughts and behaviors; (b) self-report questionnaires (e.g., depressive symptoms); (c) basal assessment of cardiac activity, and (d) a modified Trier Social Stress Test (Kirschbaum et al., 1993). The modified TSST only occurred at the initial (baseline) visit.

The procedure was as follows: Pre-speech basal cardiac activity was recorded approximately 2 hours after arrival to the laboratory and 1 hour before the TSST. Considering the effects of body posture on cardiac activity (Brindle et al., 2013; Houtveen et al., 2005), pre-speech basal RSA measures were recorded when participants were sitting and then standing, to mimic the physical requirements of the speech task. Specifically, participants were told to relax, watch an emotionally neutral video, and cardiac signals were recorded first while participants were sitting (12 minutes) and then while standing (3 minutes).

The modified TSST began about 3 hours after arrival to the laboratory. Adolescents were asked to pretend to audition for a reality show about how adolescents make friends and interact with other teens. Specifically, after a 1-minute standing preparation period, participants were asked to remain standing and give a 3-min audition speech. During the preparation and the

speech, participants were oriented toward a camera connected to a closed-circuit feedback screen displaying their own live image. A young adult male "judge" was present in the room with the female adolescent during the speech task, ostensibly evaluating the quality of the performance. The presence of an adult and opposite-sex judge was intended to increase the social–evaluative nature of the task, given that laboratory tasks that elicit social evaluation and threaten an individual's social self are known to activate stress responses, including cardiovascular parasympathetic responses (McLaughlin et al., 2014). Physiological data were obtained at baseline and during the TSST. These data allow for the examination of acute stress response of the ANS.

Measures

Suicidal Thoughts and Behaviors

Life-time suicide ideation and behaviors were assessed at baseline and then recent suicidality at each follow-up assessment (i.e., every 4 months) using the Self-Injurious Thoughts and Behaviors Interview (Nock et al., 2007). The SITBI is a structured clinical interview designed to assess a variety of self-injurious thoughts and behaviors, including suicide ideation, plans for suicide attempts, and aborted or completed suicide attempts. It does not measure or ask about imminent suicidal thoughts or behaviors.

At the initial visit, lifetime history of STB was determined by asking participants whether they had ever thought about killing themselves (i.e., "Have you ever had thoughts of killing yourself?"), made any plans to kill themselves (e.g., "Have you ever actually made a plan to kill yourself?"), or made any actual or aborted attempts to kill themselves (e.g., "Have you ever made an actual attempt to kill yourself in which you had at least some intent to die?"; "Have you ever been close to killing yourself and at the last minute decided not to kill yourself? Or, at the

last minute, someone or something else stopped you?"). A dichotomous score for lifetime STB score was then derived from participants' affirmative responses to one or more of the SITBI items to indicate 1 ("yes") for lifetime STB and participants responding "never" or "no" to all items were scored as 0 ("no") for lifetime STB.

At follow-up visits (i.e., at 4, 8, and 12 months), participants were asked about the presence of (a) suicidal ideation, (b) suicide plans, and (c) suicide or aborted attempts over the preceding four months using the same SITBI items asked at during the baseline visit. Participants' SITBI responses across the three follow-up periods (i.e., 4-, 8-, 12-months) were then aggregated into a single score to indicate any presence of suicidal ideation, plans, and/or attempts in a 12-month period. A dichotomous score for prospective STB score was then derived from participants' affirmative responses to one or more of the SITBI items to indicate 1 ("yes") for prospective STB and participants responding "never" or "no" to all items were scored as 0 ("no") for prospective STB.

Physiological Data Processing

ECG were collected using three electrodes on the chest connected with Biopac fMRI compatible wireless signal logging (Biopac Systems, USA) through Siemens' telnet MPCU, with a sampling frequency of 400 Hz. Data were converted into an ASCII formatted string of amplitude values that was then fed into Mindware HRV software (Mindware Technologies, Gahanna, OH). Trained research assistants visually reviewed ECG data for accurate identification of R-spikes and corrected data when the automated program misinterpreted the R-spikes. Each participant's HRV data were coded by at least two trained research assistants to ensure the highest level of accuracy and any individual RSA values that differed more than .05 were reconciled until agreement within a .01 difference was met. RSA was calculated in 60-

second epochs by Mindware which were then averaged across the 3-minute baseline. RSA was then calculated over the duration of the TSST speech and then averaged across the 3-minute task. Averaging across multiple epochs increases the stability of the RSA value (Zisner & Beauchaine, 2016), as opposed to analyzing the RSA epochs individually. RSA data for 19 individuals during baseline and 20 during the speech task were missing due to human error, equipment errors during sample collection, or participant's failure to complete the task (for additional details, see *Missing Data and Outliers*). All RSA values are expressed in units of log (beats/min^2/Hz).

Early Pubertal Timing

Participant biological maturation (puberty) was measured using girls' self-reported pubertal timing (i.e., youth's level of development relative to peers). To calculate early pubertal timing, pubertal status was first measured using the Pubertal Developmental Scale (PDS), which consists of five items about physical development with good psychometric properties (Petersen et al., 1988). The PDS was administered at baseline to adolescents and their primary caregiver. The indicators of pubertal development include body growth spurt, pubic hair, changes in skin (pimples), and breast growth, using a 4-point scale (1= *not started yet*, 2 = *barely started*, 3 = *definitely underway*, 4 =*seems completed*. Participants also answered whether they had started menstruating (1= *no*, 4 = *yes*). The PDS has shown strong validity and reliability in pre- and mid-adolescent female samples (Brooks-Gunn et al., 1987; Schmitz et al., 2004). The PDS measure is also significantly associated with hormonal measures and physical examinations used to estimate pubertal development (Shirtcliff et al., 2009). Cronbach alpha for the five items to create the PDS scale score used generated an intraclass correlation of a = .82.

To create an early pubertal timing index, residualized scores were created by regressing participants' PDS scale scores onto chronological age (Rudolph et al., 2014). Higher scores

indicate earlier pubertal maturation compared to same-age peers and lower scores indicate later pubertal maturation compared to same-age peers.

Data Analysis

Bivariate associations between key study variables and covariates (e.g., age, body mass index [BMI], and antidepressant medication use) first were examined with zero-order correlations. Associations between ANS physiology and STB was preliminarily analyzed using independent *t*-tests. Following, a path analysis was used to test whether participants' parasympathetic stress physiology (i.e., baseline and speech) was associated with participants' lifetime history of STB and prospective STB (12-months following the initial visit), while controlling for age, BMI, and antidepressant medication. Standing baseline, but not sitting baseline, was used as the "vanilla baseline" because participants' orthostatic posture during this period mirrored the speech task. Baseline and speech RSA scores were modeled as manifest predictors. Dichotomous measures of lifetime and prospective STB (12 months following the TSST) were regressed onto baseline and speech RSA scores (modeled as manifest predictors), while covarying age, BMI, and antidepressant medication use. Interaction terms were created from mean-centered variables to examine moderation effects

Missing Data and Outliers

For the STB variables, missing data ranged from .01% (n = 3) for lifetime STB to 10.04% (n = 23) for prospective STB. No participants' data were missing due to death from suicide or any other causes. For the baseline and speech RSA (i.e., independent) variables, there was missing data for 8.29% (n = 19) for standing baseline and 8.73% (n = 20) for the speech task. Of the missing RSA data, two participants aborted the entire TSST event (including baseline), six refused to complete the speech portion of the TSST, and 17 participants' data could not be used

due to Mindware hardware issues or human error during recording. One participant's data were excluded after they reported taking prescription heart medication for cardiomyopathy, which alters patterns of cardiac activity (cite). None of the covariates (e.g., age, BMI, medication use) had missing data.

We tested for significant differences across the covariates and RSA variables between those who did and did not complete the lifetime and prospective STB measures using *t*-tests, and our attrition analyses identified no systematic bias in the missing data. Additionally, to test for potential biases in the missing data, we ran Little's (1988) MCAR's test and the data were determined to be missing completely at random, $\mathcal{X}^2(47) = 44.47$, $p = .58$. To account for missing data in the independent variables (RSA variables), we used full information maximum likelihood (i.e., FIML) in the path analysis.

Outliers (i.e., values greater than 3 standard deviations beyond the mean) in the dependent variables were winsorized to bring the values within 3 standard deviations of the mean. Descriptive statistics and t-test analyses were run using *SPSS 28*. The path analysis was implemented using *Mplus 8.0* (Muthén & Muthén, 2018). Interaction analyses (e.g., Simple Slopes tests, Regions of Significance) were further examined using R.

Results

Descriptive Analyses

Descriptive statistics and zero-order correlations of key study variables are presented in Table 1. Overall, there was not a significant change in RSA, $t(203) = -1.41$, $p = .16$, between baseline and the speech task. Table 2 presents descriptive statistics and *t*-tests comparing baseline and speech RSA for youth who did versus did not report lifetime STB, and who did versus did not report STB across the 12-month follow-up assessments (i.e., prospective STB). At

Table 4.1 Descriptive Statistics and Zero-order Correlations of Key Study Variables

	M(*SD*)	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Age	11.80(1.80)	--								
2. BMI	22.76(5.62)	**.34*****	--							
3. Antidepressant Use	.30(.46)	**.27*****	0.12	--						
4. Pubertal Status	2.84(.87)	**.73****	**.41****	**.22****	--					
5. Pubertal Timing	0(1)	.00	**.25*****	.02	**.68*****	--				
6. Lifetime STB	.46(.50)	**.39*****	**.15***	**.55*****	**.35*****	.11	--			
7. Prospective STB	.30(.46)	**.21****	0.08	**.31*****	**.23*****	.11	**.49*****	--		
8. Baseline RSA	5.72(1.01)	**-.20****	-0.01	**-.28*****	**-.17***	-.04	**-.31*****	**-.23****	--	
9. Speech RSA	5.78(1.11)	-0.07	0.03	**-.14***	-.07	-.02	-.12	**-.15***	**.60*****	--

Note. BMI = body mass index, STB = suicidal thoughts and behaviors, and RSA = respiratory sinus arrhythmia. Antidepressant use was coded dichotomously, 0 = *no*, 1= *yes*. Pubertal status is not standardized for age. Pubertal timing represents a standardized value. All physiological measures were recorded when participants came to the lab for the TSST event. Both lifetime and prospective STB were scored dichotomously, *yes* = 1, *no* = 0. Significant correlations are in bold and denoted as **p* < .05, ***p* < .01., ****p* < .001.

Table 4.2 Means, Standard Deviations, and T-tests of Baseline and Speech RSA by Lifetime and Prospective STB Groups

	Lifetime STB				Prospective STB			
	Yes	No	T-test		Yes	No	T-test	
	M(SD)	*M(SD)*	*t(df)*	*p*	*M(SD)*	*M(SD)*	*t(df)*	*p*
Baseline RSA	**5.38(1.08)**	**6.01(.85)**	**4.70(182.80)**	**< .001*****	**5.38(1.04)**	**5.89(.99)**	**3.25(190)**	**< .001****
Speech RSA	5.63(1.13)	5.91(1.08)	1.77(207)	.08†	**5.57(1.02)**	**5.92(1.13)**	**2.09(191)**	**.04***

Note. RSA = respiratory sinus arrhythmia. Speech refers to TSST event. All physiological measures were recorded when participants came to the lab for the TSST. Both lifetime and future STB were scored dichotomously, *yes* = 1, *no* = 0. Significant findings are in bold and denoted as †$p < .10$, *$p < .05$, **$p < .01$., ***$p < .001$.

the time of the initial visit (i.e., baseline), over 53% of the sample (*n* = 123) had endorsed STB at least once in their lifetime and nearly 27% of the sample (*n* = 23) went on to endorse suicidality at least once during follow-up (i.e., 6-30 months following Time 1), with 80.6% (n = 50) of those participants having also endorsed lifetime STB. Participants who reported histories of STB produced significantly lower baseline RSA than youth without lifetime STB. Youth who later reported subsequent STB at follow-up evinced significantly lower RSA at baseline and during the speech task, compared to their peers who did not evince future STB (for full results, see Table 2). Relations between ANS physiology and measures of STB are discussed below.

Path Analysis

We implemented a path model with a binary outcome to examine whether autonomic physiology was associated with lifetime STB and predictive of prospective STB 12 months following the initial laboratory visit, while controlling for age, BMI, and antidepressant medication use. Regressions predicting to prospective STB were adjusted for participant's history of STB. Additionally, in the same model, we tested whether early pubertal timing moderated the association between RSA and STB by implementing two interaction terms (e.g., Baseline RSA X Early Pubertal Timing; Speech RSA X Early Pubertal Timing). Variables used to create the interaction terms were mean centered prior to entering them into the model. Significant odds ratios (*OR*s) less than 1 were inversed below to allow for interpretation of a positive association between independent and dependent variables. For full results, see Table 3.

Lifetime STB

As predicted, participants with lower baseline RSA evinced two-thirds greater odds of reporting a lifetime history of STB, after controlling for age, BMI, and antidepressant use, compared to those with higher baseline RSA. Also confirming predictions, earlier, compared to

Table 4.3 Concurrent and Predictive Associations Between Covariates, Early Pubertal Timing, Autonomic Physiology Scores, and Lifetime and Prospective STB: Results of Path Analysis

	Lifetime STB		Prospective STB	
Variable	*B* (*SE*)	*OR* (95% CI)	*B* (*SE*)	*OR* (95% CI)
Age	**.41 (.11)*****	**1.51 (1.26 – 1.81)**	.04 (.12)	1.04 (.86 – 1.26)
BMI	-.02 (.03)	.98 (.93 – 1.04)	.001 (.04)	1.00 (.95 – 1.06)
Medication Use	**2.76 (.47)*****	**15.82 (7.34 – 15.82)**	.19 (.42)	1.21 (.61 – 2.42)
Early Pubertal Timing	**.40 (.20)***	**1.50 (1.07 – 2.09)**	.26 (.21)	1.29 (.91 – 1.83)
BL RSA	**-.51 (.24)***	**.60 (.41 - .88)**	-.02 (.23)	.98 (.67 – 1.44)
Speech RSA	.17 (.21)	1.19 (.84 – 1.68)	-.23 (.22)	.79 (.55 – 1.14)
BL RSA X PT	.19 (.29)	1.20 (.75 – 1.94)	-.06 (.26)	.95 (.61 – 1.46)
Speech X PT	-.33 (.23)	.72 (.49 – 1.06)	.37 (.21)†	1.44 (1.02 – 2.04)
LT STB	--	--	**2.26 (.46)*****	**9.58 (4.53 – 20.29)**

Note. RSA = respiratory sinus arrhythmia. Speech refers to TSST event. All physiological measures were recorded when participants came to the lab for the TSST. Baseline and Speech RSA represent mean-centered values. Both lifetime and future STB were scored dichotomously, *yes* = 1, *no* = 0. Significant paths are in bold and denoted as †$p < .10$, *$p < .05$, ***$p < .001$.

later, pubertal timing was associated with greater odds of endorsing a lifetime history of STB. Additionally, being older and using antidepressants were also significantly associated with increased odds of reporting a history of suicidality. Contrary to hypotheses, early pubertal timing did not significantly moderate the relation between either baseline or speech RSA and lifetime STB.

Prospective STB

To our surprise, and contrary to predictions, neither baseline nor speech RSA were significantly predictive of prospective STB. Additionally, early pubertal timing was not independently predictive of later endorsement of suicidality. Confirming an abundance of past research (see Franklin et al., 2017), endorsing a history of STB increased odds of endorsing prospective STB by nearly tenfold, which is not surprising given that over 80% of youth who had histories of suicidality later endorsed STB in the 12 months following the initial visit. Contrary to predictions, early pubertal timing did not significantly moderate the association between baseline RSA and prospective STB; however, the Speech RSA X Early Pubertal Timing interaction term approached significance (p = .08). As one of the main aims of this study was to investigate whether pubertal timing moderated the link between parasympathetic activation and STB, this interaction was probed further to examine the borderline effect using simple slopes analyses and a regions of significance test.

Regions of Significance and Simple Slopes

To further dissect the Speech RSA X Early Pubertal Timing interaction, simple slopes analyses (Aiken et al., 1991) were plotted using ± 1 SD from the mean (see Figure 1). The simple slopes analyses revealed that, for adolescents with lower (later) pubertal timing, greater speech RSA was associated with less risk of prospective STB, b = -.10, SE = -2.62, p < .05. For

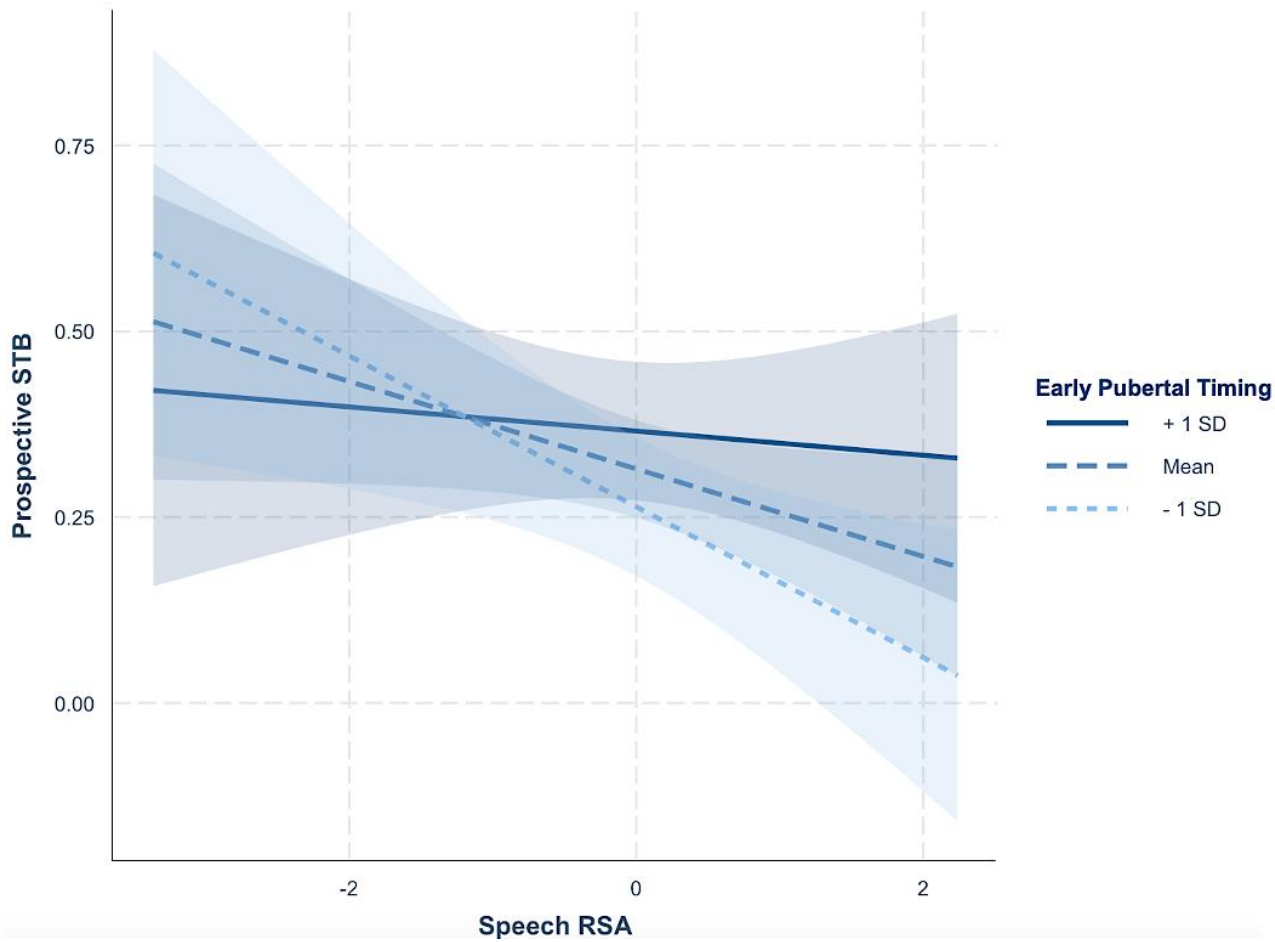

Figure 4.1 Interaction effect between participants' mean RSA during the speech task and early pubertal timing on the odds of prospective STB 12-months following the initial visit. RSA = respiratory sinus arrythmia and STB = suicidal thoughts and behaviors. Speech RSA was centered to aid interpretation and early pubertal timing represents a standardized score. STB is dichotomously coded, 1 = *yes*, 0 = *no*.

adolescents with higher (earlier) pubertal timing, overall speech RSA was not significantly related to prospective STB, b = -.02, SE = .04, p = .67. Therefore, greater PNS activity during the speech predicted less likelihood of reporting STB over the next 12 months only for girls who had relatively later pubertal timing.

Next, we used a regions of significance test to identify more precisely at which point in pubertal timing the relation between prospective STB and speech RSA was significant (see Figure 2). The regions of significance define the specific values of early pubertal timing at which the slope of the regression of prospective STB on speech RSA transitions from non-significance to significance ($p < .05$). The regions of significance analyses indicated that when early pubertal timing is inside the interval [-14.32, -.04], the slope of speech RSA is significantly ($p < .05$) and negatively related to prospective STB. The range of observed values for standardized early pubertal timing is -2.61 to 3.96. Therefore, speech RSA was negatively associated with prospective STB throughout average to later pubertal timing. Conversely, for girls with average to early pubertal timing, RSA during the speech was not significantly predictive of future reporting of STB.

Discussion

Despite the growing prevalence of suicidality in adolescents, few studies have used longitudinal models to examine prospective STB risk across the pubertal transition. Additionally, very little is understood about how pubertal timing moderates autonomic stress physiology to either buffer against or increase vulnerability for suicidal ideation, plans and attempts during early adolescence. This work sought to address these scientific gaps by using an interpersonal stress paradigm coupled with a prospective design to examine parasympathetic stress responses

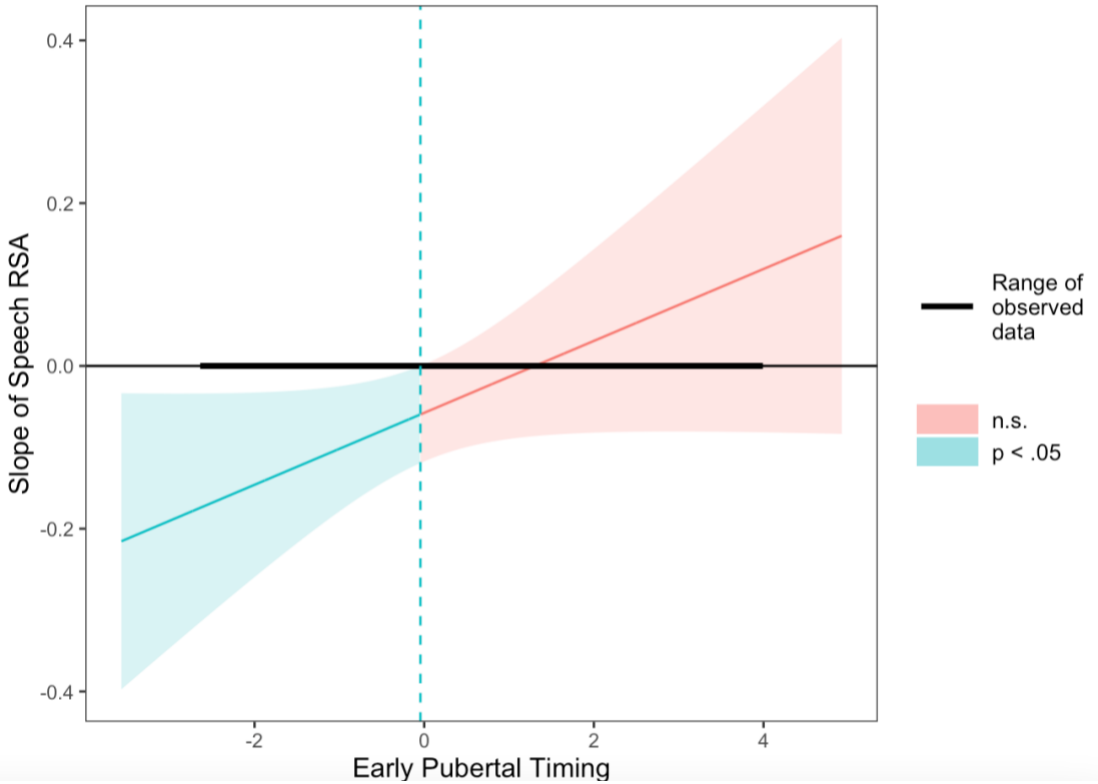

Figure 4.2 Johnson-Neyman plot of the Regions of Significance of the simple slope showing the relation between prospective suicidal thoughts and behaviors (STB) and speech RSA as a function of early pubertal timing. The region of significance defines the specific values of pubertal timing at which the slope of the regression of prospective STB on speech RSA transitions from non-significance to significance. STB is dichotomously coded, 1 = *yes*, 0 = *no*.

and pubertal timing as concurrent and longitudinal predictors of STB in a sample of psychiatrically high-risk adolescent females. Overall, our findings confirmed that low baseline RSA and earlier pubertal timing are both independent contributors to increased risk for concurrent STB in clinically high-risk adolescent females. Additionally, we found a borderline effect for the interaction between speech RSA and pubertal timing predicting subsequent STB, suggesting that later, compared to earlier, biological maturation in females moderates the association between parasympathetic stress activation to a social challenge and risk for subsequent suicidality. Findings and clinical implications are discussed below.

Baseline RSA and Lifetime STB

As hypothesized, participants with lower baseline parasympathetic activity (i.e., RSA) had greater odds of endorsing a lifetime history of STB. Our findings replicate past research in which parasuicidal adolescent females evinced lower baseline RSA compared to healthy controls (Crowell et al., 2005), however, other studies have failed to find similar associations with between tonic RSA and adolescent STB (Giletta et al., 2017; James et al., 2017; Wielgus et al., 2016; Yang et al., 2019). Sample differences may account for the varying findings across studies. The participants in this study, and those included in the Crowell et al. (2015) study, both were psychiatrically high-risk with documented histories of suicidal ideation and suicide attempts, self-injury, and/or depression, compared to related studies that either included community samples (James et al., 2017; Wieglus et al., 2016). Indeed, clinical samples may evince more exaggerated physiological activity compared to non-clinical samples (Beauchaine, 2015), and this phenomenon has also been demonstrated in depressed children who display lower basal RSA compared to their healthier peers (Pang & Beauchaine, 2013). Studies with clinical samples of adolescents are more similar to studies of RSA and psychopathology in adults. In predominantly

clinical samples of adults, lower baseline PNS activity has been associated with depression (Bylsma et al., 2014; Kemp et al., 2014; Licht et al., 2008; Yaroslavsky et al., 2014), suicidal ideation (Chang et al., 2017; Rottenberg, 2007) and suicide attempts (Wilson et al., 2016). Thus, the association of baseline RSA with suicidality may reflect a clinically relevant biomarker that emerges early in adolescence and persists into adulthood.

In line with past research, reduced tonic RSA is a marker of poor emotion regulation for a number of psychiatric problems, including depression and anxiety (Beauchaine, 2001; Pang & Beauchaine, 2013). Self-regulation capacities are crucial for successful interpersonal engagement throughout development, however, the ability to tolerate distress and manage affective responses are vital during adolescence when establishing peer relationships is prioritized (Rubin et al., 2006). For those who lack these adequate coping skills, engaging in suicidal thinking or behaviors may result from an inability to tolerate distress. The exact mechanisms linking resting state autonomic function and STB remain poorly understood, but our findings provide additional evidence for low baseline RSA as an independent contributor to increased risk for STB and as a possible biomarker for past suicidality.

Early Pubertal Timing and Lifetime STB

We also examined whether pubertal timing would differ for girls who had endorsed past STB versus those who did not. As predicted, girls with earlier, compared to later, pubertal timing evinced the greatest odds of reporting prior suicidality. In a longitudinal study of Norwegian adolescents, both early pubertal timing and being female independently increased odds of a suicide attempt across a two-year follow-up (Wichstrøm, 2000). No other research, to our knowledge, has found an association between early pubertal timing and STB, as most research has focused more broadly on depression (Galvao et al., 2014) or overall psychopathology

(Graber, 2013). However, early menarche has been linked with increased risk for suicidal ideation in adolescent females (Lee et al., 2020; Nacinovich et al., 2016; Stice et al., 2001) and appears to increase risk for STB through early adulthood (Roberts et al., 2020). Researchers have theorized that other factors that may be related to girls entering puberty earlier relative to peers, such as early childhood adversity (Belsky, 2019), may also be associated with the onset and development of STB (Ho et al., 2022). If early life adversity indeed drives both early pubertal timing and increased risk for STB, family-level interventions could possibly mitigate this trajectory, however, additional research is needed to better understand this theorized association.

We do know that there are greater social costs associated with early puberty for girls, compared to boys, in that they physically deviate from their peers at a time where social conformity is greatly desired (Rudolph et al., 2014). Further, girls with actual or perceived early pubertal maturation report low self-esteem and poor body image (Beauchaine, 2001; Benjet & Hernández-Guzmán, 2002; Pang & Beauchaine, 2013; Tobin-Richards et al., 1983; Williams & Currie, 2000), both of which have been identified as risk factors for STB in adolescent females (Brausch & Muehlenkamp, 2007; McGee & Williams, 2000). Our study further corroborates that early pubertal timing is an independent contributor to STB risk in female youth and may partially explain the long-standing sex differences in rates of adolescent STB.

Pubertal Timing, Speech RSA, and Prospective STB

Contrary to hypotheses, neither baseline nor speech RSA were independently related to prospective STB, however, our analyses revealed a near significant (p = .08) interaction between speech RSA and pubertal timing, and exploratory analyses were performed to probe the moderation effect. When examined using simple slopes and regions of significance analyses, we found that increases in RSA during the speech (i.e., augmentation) were associated with fewer

odds of prospective STB, but only for adolescents with later pubertal timing. In other words, RSA augmentation in response to a social challenge was protective against risk for prospective STB but only for girls who enter puberty later, compared to earlier, relative to peers.

Blunted parasympathetic responses, typically shown as no change in RSA or mild RSA augmentation in response to a stressor, have been independently associated with both concurrent and prospective STB in children and adolescents (Gonzalves et al., in prep; James et al., 2017; Yang et al., 2019). Moderate RSA withdrawal in response to a stressful or threatening situation is considered adaptive, allowing for the fast-acting SNS to mobilize the body to respond to the environment (Hastings & Kahle, 2019). Thus, the current findings seem counter-intuitive, but they may reflect the idea of neuroception (Porges, 2007). An RSA increase in response to a social challenge could be adaptive if the individual found the task engaging, not threatening, and would signal an orientation response supportive of calm approach behaviors (Hastings et al., 2008); however, RSA augmentation is maladaptive if the individual found the task demanding or stressful, necessitating a withdrawal response (Porges, 2003). Considering that higher speech RSA was a protective, as opposed to a risk, factor for future STB dependent on pubertal timing suggests that some adolescents who entered the pubertal transition later, compared to earlier-maturing peers, were buffered by finding the speech task to be non-threatening. Just as females who experience atypically early puberty are at greater risk for depression (Stice et al., 2001), girls who are later in their biological development may benefit from delayed physical changes and a slower entrance into the physiological cascade that foments greater vulnerability for psychopathology.

Limitations and Future Directions

This study is the first, to our knowledge, to examine the associations between pubertal timing, parasympathetic stress physiology, and concurrent and prospective STB in a sample of clinically high-risk female adolescents. Despite the many strengths of this research, there are certain limitations that should be considered in light of our findings. First, this analysis did not include measures of the SNS at baseline or during the speech. Including an index of adolescents' sympathetic activity allows for a comprehensive view of the ANS stress response (El-Sheikh et al., 2009) and could further contextualize the RSA findings (e.g., PNS augmentation in the presence of SNS activation could signal a failure to modulate stress levels). Second, although examining adolescent suicidality as a dichotomous measure of STB is common (Crowell et al., 2005; Wieglus et al., 2016; Yang et al., 2019), it would be beneficial to test whether certain physiological profiles, as well as different levels pubertal timing, were more or less predictive of suicidal ideation versus suicide attempts. Youth who never go beyond ideating may represent a different population than youth who eventually make actual or aborted attempts, and so it would be beneficial to study these outcomes separately. Third, although the TSST reliably elicits stress related to individual performance and judgment by others (Kirschbaum et al., 1993), examining stress related to peer or family conflict may better represent precipitating events that have been reported by youth who engage in STB (Orlins et al., 2021). Fourth, relatively few girls reported STB at the follow-ups, and most who did so had previously endorsed STB, which limited the opportunity to assess unique prospective associations between RSA or pubertal timing and future STB. Lastly, sexual minority youth and transgender youth are at heightened risk for STB (Miranda-Mendizabal et al., 2019), and although we did not test for group differences based on

sexual orientation and gender identity, future research should consider both and would benefit from their inclusion.

Conclusion

Adolescence represents a unique period of vulnerability, considering the simultaneous changing of multiple physiological systems and the reorganization of the social network and social roles (Miller & Prinstein, 2019). There is significant overlap in biological vulnerabilities and psychosocial risk factors related to suicidal ideation and behaviors (Crowell et al., 2014) and furthering our understanding of how pubertal processes influence suicide risk will not only benefit early detection but allow for the creation of interventions that are sex- and age-specific (Ho et al., 2022). Our findings of reduced baseline RSA and early pubertal timing demarcating girls with histories of STB provide support for past research that suicidal youth exhibit poor emotion regulation and early menarche signaling a greater risk for psychopathology. Luckily emotion regulation skills are teachable and early puberty is easily identifiable, suggesting both risk factors present opportunities for realistic interventions. Additionally, identifying potential biomarkers for increased vulnerability for STB presents the opportunity for objective assessments of future risk and researchers should continue to approach adolescence as period of great consequence if youth do not receive the support they need.

CHAPTER FIVE

GENERAL DISCUSSION

Adolescent suicide is one of the top causes of death for youth in the U.S. (Hoffman et al., 2020), yet it remains a relatively rare event (Roh et al., 2018; Wasserman et al., 2005), making its accurate prediction inherently and methodologically challenging (Cha et al., 2018). However, STB are common (Ivey-Stephenson et al., 2020; Lawrence et al., 2021) and present a more realistic and generative opportunity for research and intervention, given how many youth engage in suicidality at various levels (Nock et al., 2013). Decades of empirical investigation have revealed that female adolescents and youth of color are at greater risk of engaging in STB compared to their male and Euro-American counterparts, respectively (Kann et al., 2018; Nock et al., 2013). Moreover, despite the ongoing effort to identify both distal and proximal risk and protective factors across all adolescent populations, suicidality rates in the U.S. continue to climb (Ivey-Stephenson et al., 2020). Much of past research utilized cross-sectional and correlational designs, without the inclusion of objective physiological variables (Cha et al., 2018; Miller & Prinstein, 2019). This program of research aimed to elucidate key psychosocial and neurobiological correlates for engaging in past and prospective STB among Mexican-origin youth and ethnically diverse female adolescents with histories of depressive symptoms and suicidality.

Main Conclusions

In Paper 1, Mexican-origin youth who reported greater family and peer conflict also showed a higher prevalence of STB across adolescence, and particularly during the transition into high school. Additionally, girls and youth with later generation status evinced greater suicidality from early to late adolescence. Conversely, Mexican-origin youth who reported a high

degree of familism were buffered from both concurrent and prospective STB (up to one year later). In Paper 2, in Mexican-origin youth with elevated but sub-clinical depression symptoms, histories of STB were associated with lower baseline and task (i.e., during social exclusion) SNS activity, compared to peers without STB. Youth who evinced overall lower baseline ANS activity paired with greater ANS stress activation (i.e., increases in both SNS and PNS) had greater odds of endorsing STB in the two years following their initial study visit. Lastly, in Paper 3, lower baseline parasympathetic activity and early pubertal timing independently demarcated clinically high-risk girls with a history of STB from their peers with no past suicidality. Many of the participants who had reported prior STB also engaged in subsequent STB during the 12-month follow-up. However, girls with later pubertal timing and who displayed higher parasympathetic activation during the performance task were buffered from endorsing prospective STB. Based on these outcomes, I will discuss overall conclusions, clinical implications, and future directions for adolescent suicidality research.

First, these findings demonstrate that suicidal ideation (SI) in youth is fairly common, even among samples who have not been identified as "high-risk". Although SI was not disentangled from suicide plans or attempts in the final analyses, the majority of youth in each study who endorsed any STB reported suicidal thoughts, more so than the other indicators. This is reflected in other research. For example, in a community sample of pre-adolescent children as young as 9- and 10-years-old, nearly 15% reported a lifetime history of SI and only one-third of those youth had received any psychiatric treatment (Lawrence et al., 2021). Among high school students, national prevalence rates for SI increase to nearly 19%, suggesting that 1 in 5 adolescents in the U.S. has seriously considered suicide (Ivey-Stephenson et al., 2020). Compared to 12% of U.S. individuals who have reported serious thoughts of suicide during

adulthood (Czeisler et al., 2021), the pre-, peri- and post-adolescence years are a vulnerable period for heightened STB risk, and this was further corroborated by this dissertation.

Second, familial relationships are crucial for the psychological wellbeing of adolescents in general, and perhaps especially for youth of Mexican origin. Within the present body of research, only Paper 1 included psychosocial predictors, primarily focused on the quality of the participant's interpersonal relationships (e.g., peer conflict, family conflict, familism). It was the familial, compared to the peer, relationships and values that were more predictive of both concurrent and prospective STB across the 8 years of the study. This finding was somewhat surprising considering that the adolescent years are when many youth individuate from their parents and prioritize friends (Rubin et al., 2011). Further, the protective factor of familism was the only psychosocial measure that was associated with prospective STB across the transition into and through the end of high school. These results suggest that Mexican-origin adolescents' sense of obligation to their families influences their risk for psychopathology, with youth who manifest a greater sense of familial responsibility being buffered from suicidality. As demonstrated by past research (Garza & Pettit, 2010; Umaña-Taylor et al., 2011), a high degree of familism is especially protective during times of psychological distress, when adolescents might consider STB, and a strong connection to family offers a powerful reason to live.

Third, the transitions into puberty as well as starting high school both present periods of elevated risk for psychopathology. The pubertal transition is a well-established risk period for engaging in suicidality (Ho et al., 2022), as many biological, social, and physical changes take place that present new challenges for youths' adaptation and adjustment (Dahl & Gunnar, 2009; Spear, 2009). Paper 3, which focused on pre-, peri-, and post-pubertal females, demonstrated that age and pubertal timing were positively associated with lifetime and prospective STB,

suggesting that girls who were more biologically mature also reported greater levels of suicidality. Our finding that early pubertal timing increased odds of girls' endorsing prior STB also suggests that *when* biological maturation occurs, relative to peers, plays a critical role in the development of psychopathology, replicating past research (Wichstrøm, 2000). Typically following the onset of puberty, youth transition into high school (e.g., around ages 14- to 15-years-old) and this passage marked a period of peak onset for STB prevalence for the youth in Paper 1, mirroring past research (Nock et al., 2013). Although not a biological transition like that of puberty, starting high school does represent a time of great social change as friendships shift and youth are faced with greater academic independence. Together, this evidence further illustrates the importance of early identification of youth who may be at risk of developing STB both during the pubertal transition and when starting high school.

Fourth, the results from Papers 2 and 3 provide further confirmation that youth who engage in STB are demarcated by unique physiological activity, and these neurobiological profiles may differ depending on the clinical risk of the individual. For example, in Paper 2, among a mildly at-risk but not clinically affected group of Mexican-origin adolescents, those with a history of STB displayed lower sympathetic, but not parasympathetic, activity both at baseline and during a social challenge task. Conversely, the clinical sample of girls in Paper 3 displayed lower baseline parasympathetic activity compared to peers without STB (however, SNS was not measured). There is research with adults and adolescents which supports each paper's findings (Crowell et al., 2005; Thorell et al., 2013; Yang et al., 2019), but understanding the neurobiological differences between sub-clinical and clinical adolescent groups requires additional research. Further, basal ANS hypoactivity paired with greater ANS activation during the challenge was predictive of greater odds of subsequent STB for the youth in Paper 2, whereas

we did not find a main effect of task-responsive PNS activity predicting prospective STB in Paper 3. Additionally, the acute stress activity displayed by the youth who later engaged in STB did not mirror adaptive or reflexive responses (Porges, 2007); rather, those responses were indicative of individuals ill-equipped to tolerate the challenges they were facing in each study (Miller & Prinstein, 2019). What can be concluded is that the adolescents who eventually endorsed STB following the initial assessments looked physiologically different than their peers who did not, and that the physiological characteristics that convey risk for non-clinical and clinical samples of youth may differ.

Clinical Implications

Translating empirical findings into practical applications is an ongoing challenge for researchers and can often take years. However, there are several key takeaways from this body of research that could inform clinical practice today. To begin, suicidality among adolescents is unfortunately a common occurrence and should be addressed as early as possible. Universal screening is currently in place for children as young as 10-years-old in some hospitals (Thom et al., 2020), but this threshold should be lowered to include younger children. Furthermore, medical and mental health professions should provide parents with psychoeducation about the warning signs of STB in children and adolescents, especially as it may differ by age. Next, the roles of family conflict and obligation should be considered when assessing Mexican-origin youth for suicide risk. Given the documented importance of the family unit, Mexican-origin youth should be asked about conflicts with parents during psychiatric assessments, but also about their sense of connectedness and responsibility to members of their family. Following, teachers, nurses, physicians, and other providers who encounter children and adolescents should be educated on the heightened risk for psychopathology associated with the pubertal transition and

when youth start high school. Many of these professionals are tasked with intervening during moments of crisis, but often lack the adequate tools to support both youth and their families. Expanding training across schools, clinics, and hospitals could produce a larger network of adults who can spot the warning signs of STB. Lastly, as biological technology advances and becomes more accessible, it is worth considering the use of physiological assessment when examining those with known or suspected histories of suicidality. We are likely years away from confirming precise biomarkers for STB but, given that so many risk factors for suicide are transdiagnostic and nonspecific (Miller & Prinstein, 2019), including an objective biological measure in psychiatric assessments may help clinicians identify youth who are at the greatest risk.

Future Directions

The field of adolescent suicidality research is still relatively small, but as this public health crisis continues to persist, empirical investigations will need to expand to address the varying complexities of STB prediction and early intervention. To date, very few adolescent suicidality studies are longitudinal. To improve prediction precision and better understand which youth are at risk of developing STB, additional multi-wave assessments are needed to follow youth across time. Moreover, adolescent suicidality studies that incorporate neurobiological measures are rare, and given the importance of objective, biological assessments in identifying risk for psychopathology, future research should consider including psychophysiological indices. Additionally, it will be important to include measures of multisystem stress physiology (e.g., ANS and HPA), in order to produce a comprehensive report of an individual's biological response to stressors, which may provide further insights into other risk factors. Continuing, future studies should utilize both psychosocial and neurobiological indices which would

facilitate moderation analyses. For example, youth exposed to certain adverse life events who also display dysregulated stress responses may be at particularly increased risk for psychopathology. Understanding these associations will be crucial for informing both research and practice.

Given the pubertal timing findings, it would benefit forthcoming studies to also incorporate pubertal maturation indices (e.g., status, tempo, timing) to facilitate a deeper investigation of how biological maturation trajectories are related to the emergence of STB. Lastly, interventions aimed at stemming the growing tide of youth and adolescent STB must be age-, gender-, and cultural-specific, but clinical research must first provide the empirical rationale for advocating for this expansion in practice. Suicidality among youth is a devastating phenomenon and one that requires a great deal more empirical interest and investment if the scientific field is going to effectively advocate for change that could save many lives.

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