



## Preliminary evidence for increased parasympathetic activity during social inclusion and exclusion in adolescents with functional abdominal pain



Marco Daniel Gulewitsch<sup>a,\*</sup>, Aiste Jusyte<sup>b,1</sup>, Nazar Mazurak<sup>c</sup>, Katja Weimer<sup>c</sup>, Michael Schönenberg<sup>a</sup>

<sup>a</sup> Department of Psychology, Clinical Psychology and Psychotherapy, University of Tübingen, Germany

<sup>b</sup> LEAD Graduate School & Research Network, University of Tübingen, Germany

<sup>c</sup> Department of Internal Medicine VI/Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Germany

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### ABSTRACT

**Objective:** Peer victimization (e.g. social exclusion) has been shown to be associated with physical health problems such as functional somatic complaints and especially symptoms of pain. To date, no study has investigated the mechanisms underlying this association in clinical pediatric samples. The aim of this study was to evaluate the parasympathetic activity during a social exclusion experience in adolescents with functional abdominal pain (FAP).

**Methods:** Twenty adolescents with FAP and 21 matched healthy participants were compared regarding parameters of parasympathetic activation before, during, and after participating in the Cyberball-game, a well-established paradigm to induce social exclusion.

**Results:** Adolescents with FAP showed an increase in parasympathetic activation during both consecutive phases of the Cyberball game (inclusion as well as exclusion condition) whereas the healthy control group remained stable. There were no differences in subjective experience of in- and exclusion between the groups.

**Conclusion:** The parasympathetic activation pattern may indicate altered processing of social stimuli in adolescents with FAP.

### 1. Introduction

Integration into peer groups is crucial for the individual development during adolescence. The transition period from childhood to adolescence is characterized by increasing time spent with peers and a significant decrease of time spend with parents [1,2]. Thus, it is not surprising that the development from childhood to adolescence is also marked by growing concerns how one is perceived by peers as well as an increased sensitivity to social exclusion [3,4]. Peer victimization during adolescence can take various forms, including direct bullying behaviors with open attacks on the victim (e.g., teasing, physical aggression) as well as more indirect manifestations such as social isolation, rejection, and exclusion from the group [5–7]. Recent meta-analyses demonstrated that peer victimization represents both an antecedent and a consequence of internalizing and externalizing mental health problems in children and adolescents [8,9]. It has also been associated with physical health problems such as functional somatic complaints and especially symptoms of pain e.g., pediatric functional

abdominal pain (FAP) [10–12], a prevalent functional gastrointestinal disorder (FGID). Despite this evidence, no study to date has directly investigated the mechanisms underlying the association between peer victimization - especially social exclusion - and functional somatic complaints in clinical pediatric samples.

Previous research has established that neural processing of both, physical and social/affective pain, are governed by partly overlapping neural substrates [13]. The association between physical and social/affective pain is probably mediated by the autonomic nervous system (ANS). For instance, pain-related FGIDs such as irritable bowel syndrome (IBS) in particular, have previously been linked to ANS imbalance and dysfunction [14–16]. The role of ANS alterations is discussed in terms of etiology and maintenance of FGIDs. It has been suggested that these disorders are related to perturbations in the brain-gut interaction and that they are influenced by reciprocal biological and psychosocial processes [17,18]. Whereas the ANS and the hypothalamic-pituitary-adrenal (HPA) axis are thought to be crucial mediators of the bidirectional brain-gut interaction [18] in adult IBS, the research on

\* Corresponding author at: Department of Psychology, Clinical Psychology and Psychotherapy, University of Tübingen, Schleichstraße 4, 72076 Tübingen, Germany.

E-mail address: [marco-daniel.gulewitsch@uni-tuebingen.de](mailto:marco-daniel.gulewitsch@uni-tuebingen.de) (M.D. Gulewitsch).

<sup>1</sup> Equal contributions.

FGIDs in children is scarce. However, there is first evidence for ANS and HPA axis disturbances in pediatric FAP and/or IBS [16,19,20].

Based on these observations, alterations of the ANS may represent a link between peer victimization - especially social exclusion - and FGIDs. In healthy individuals, unexpected social rejection is associated with an immediate response of the parasympathetic nervous system in terms of a transient cardiac slowing. This was demonstrated in adults [21–24] and adolescents [25]. Parasympathetic activation over time periods in the range of minutes has also been reported in response to social exclusion [26]. This reaction pattern is in accordance with the notion that increased parasympathetic activation reflects processing of emotions and self-regulatory effort [27]. More precisely, parasympathetic activation in response to challenging demands may indicate increased emotional processing which could facilitate adaptive social behavior and affective responses [28,29]. This assumption is in accordance with the neurovisceral integration model [30] which posits that parasympathetic activation can indicate the functional integrity of the neural networks implicated in emotion-cognition interactions.

However, experimental research on the ANS reaction to social exclusion has been largely carried out in healthy participant groups. Given the overlap of the neural response to social and physical pain [13], there is grounds to assume that individuals with chronic pain might also be particularly sensitive to distressing social experiences such as exclusion. This may be especially true for adolescents, since positive peer evaluation is of particular importance for this age group [31] and peer-victimization has been shown to be a considerable developmental risk [8,9]. Despite assumptions that social stress may exacerbate somatic symptoms in clinical groups suffering from pain disorders [e.g. 32], the mechanisms mediating this relationship are not well understood. Studies on clinical samples are lacking and most importantly, no study to date has addressed these questions in clinical samples of adolescents. This knowledge is highly relevant, as chronic pain during this developmental period has been associated with impairments in academic achievement and school absenteeism [33] and with a considerable risk for an unfavorable long-term course [34].

Therefore, the present study aimed to examine the parasympathetic reaction during social exclusion in healthy adolescents and those suffering from FAP, which is one of the most prevalent pediatric pain conditions [35]. To experimentally induce social exclusion, we employed the Cyberball game, an ecologically valid, established paradigm based on a virtual ball-tossing game in which participants are included or excluded [36,37] from peers. Given a higher vulnerability for the negative impact of social exclusion in adolescents with FAP [e.g. 10] and based on previous studies on ANS function following social rejection or exclusion [e.g. 25,26], we expected an increased parasympathetic activation during social exclusion in both groups but significantly more pronounced in adolescents with FAP as compared to controls.

## 2. Methods

### 2.1. Participants

The pediatric Rome-III criteria (36) for FAP were used as inclusion criteria for the experimental group. According to the criteria, participants were included if they experienced episodic or continuous abdominal pain at least once a week for two months or more with no evidence of an underlying organic disease. The absence of potential organic factors had to be confirmed by the managing pediatrician or gastroenterologist prior to inclusion. Twenty-one adolescents with FAP (mean age = 11.65 years, SD = 1.97; 57.1% female) were recruited via public announcements in local newspapers and at pediatricians' offices. Healthy control participants were selected to match gender and age of the FAP group. The control group was also recruited through newspapers announcements and pamphlets. All participants received two cinema coupons as reimbursement.

All adolescents and their parents gave informed consent to participate in the study. The study protocol was approved by the ethics committee of the University Hospital Tübingen.

### 2.2. Questionnaires

To characterize both groups, parents' ratings of behavioral and emotional problems were inquired with the Child Behavior Checklist 4/18 (CBCL) [38]. The CBCL is a screening instrument based on 113 items concerning behavior and emotional problems during the past 6 months. We employed the three major scores of internalizing difficulties, externalizing difficulties, and total difficulties.

Children's Rejection Sensitivity Questionnaire (CRSQ) [39], an 18-item self-report, consisting of the subscales "Anxious Expectations of Rejection" and "Angry Expectations of Rejection" was used to measure the adolescent's social rejection sensitivity.

Maturity stage was assessed by self-reports using standardized drawings representing the five Tanner-stages of pubertal development [40,41]. Additionally, height and weight were recorded and the body mass index (BMI) was calculated.

### 2.3. Experimental procedure

Participants were not briefed about the objective of the study. After arrival at the laboratory, electrocardiogram (ECG) electrodes were placed in lead II on participants' chests. Subsequently, the adolescents were asked to fill out several questionnaires prior to the experimental assessment in order to give them the opportunity to adapt to the laboratory setting. The experimental procedure started with a 5 min baseline period in which the participants were instructed to relax while seated in a chair. Following this, the Cyberball game was introduced and the participants were instructed that they would play a real-time, online ball-tossing game with two other adolescents who are located in the laboratories next door. Photographs of a total of six model identities (3 females) of child models with neutral facial expressions were selected from the Radboud faces database [42] in order to serve as supposed co-players in Cyberball game. The game display included two other players (neutral facial expression) and an avatar representing the participant (see Fig. 1). The participants were instructed to catch the virtual ball when it was thrown toward them and to subsequently toss it to another player. The game consisted of two conditions: in the first condition (social inclusion) the participants received the ball roughly one-third of the time from their co-players (includers). The inclusion as well as the exclusion condition each comprised a total of 30 throws (between 1:23 to 2:57 min) and was each followed by a short rating of the current mood (for details see below). In the second round of Cyberball (social exclusion) the participants only received the ball in the first two initial passes and were subsequently excluded for the remainder of the game. The depicted co-players were neutral pictures of one male and one female model identity that were randomly chosen for each condition and participant. The remaining two models identities were included in the manipulation check ratings for control purposes in order to implement a social stranger condition. Directly after the second round of Cyberball, a two minute recovery period (relaxing in a chair) followed. Participants were debriefed at the end of the experimental session.

### 2.4. Measurement of subjective experience and manipulation check

To assess whether the Cyberball Game manipulation exerted expected effects on the participants' mood and perception of the players, several short rating assessments were implemented during the experiment: 1) baseline assessment 2) an assessment following the social inclusion and 3) following the social exclusion Cyberball game condition. The assessments included a rating of the current mood (four-items: good/bad, happy/sad, relaxed/tense, and friendly/unfriendly

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