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*RETh*ink Online Video Game for Children and Adolescents: Effects on State Anxiety and Frontal Alpha Asymmetry

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Abstract
Emotional disorders affect numerous children and adolescents worldwide; thus, developing accessible prevention tools to reduce associated burden in youths is of crucial importance. We conducted a randomized controlled study to examine the effects of the newly developed *RETh*ink therapeutic game on reducing the subjective emotional reactivity to a stressor in children and adolescents and in modulating their frontal EEG asymmetry. A number of 165 children and adolescents were randomly assigned to one of three conditions: *RETh*ink game, a Rational Emotive Behavior Education (REBE) intervention, or a Waitlist. Participants were asked to complete an impromptu speech twice, before and after the interventions, while their anxiety and brain activity were recorded. Results suggest that relative to the Waitlist and REBE interventions, the *RETh*ink game was effective in reducing biological reactivity manifested by children and adolescents in response to speech, but not for modulating subjective anxiety. Present results provide further evidence for the potential benefits of therapeutic games in promoting mental health in children and adolescents.

Keywords Therapeutic video games · Anxiety · Prevention · Alpha asymmetry · Emotional dysregulation

Introduction

Worldwide, between 10 and 20% of children and adolescents experience mental health difficulties (Kieling et al. 2011), with anxiety disorders as the most common psychiatric conditions (Beesdo et al. 2009; Merikangas et al. 2010). Research pointed out that

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during this period of life, children and adolescents demonstrate an increased sensitivity to social evaluation, marked by a heightened stress response in the face of social and performance situations (van den Bos, de Rooij, Miers, Bokhorst, & Westenberg, 2014). These stress-related disorders represent a major burden for children and adolescents and their families, significantly impairing their psychological, emotional, and social functioning, as well as their academic achievement on a daily basis (Kessler et al. 1995; Rao and Chen 2009). Moreover, despite the short-term negative consequences, emotional disorders in childhood and adolescence are related to an increased risk for mental disorders in the long run, along with other associated disabilities, like health problems, substance misuse, and other life-threatening behaviors (Copeland et al. 2007; Fryers and Brugha 2013; Groenman et al. 2017; Lehrer et al. 2006).

Therefore, developing and disseminating effective prevention interventions, in an effort to reduce the prevalence and incidence of mental disorders and diminish other stress-related difficulties among this age category, are of crucial importance. However, even though efficient prevention interventions and programs exist (Weisz et al. 2005), more than a half of children and adolescents with any mental health difficulties fail to receive treatment due to diverse barriers (e.g., economic deficit, policy-based deficiency, inadequate delivery methods, stigma, time constraint) (Belfer 2008; Bijl et al. 2003; Kataoka et al. 2002; Patulny et al. 2013).

In spite of the widespread recognition of the importance of evidence-based prevention programs for children and adolescents, there is a major gap between needs and available resources. These alarming findings of substantial gaps in mental health resources emphasize the need for enhanced efforts to develop innovative cost-effective interventions adapted for this age category. Primarily, to address these gaps, the implementation of preventive strategies needs the adoption of a framework that goes beyond the traditional delivery model to a more adapted and engaging model that can improve the access of children and adolescents to these effective mental health services.

One potential solution from the multiple models of delivery which is becoming increasingly recognized and promising is the use of therapeutic games (Kazdin and Blase 2011). A growing number of therapeutic video games were recently developed to help children and adolescents with mental health difficulties (e.g., Personal Investigator; Coyle et al. 2009; SPARX, Merry et al. 2012). Recent research points towards the effectiveness that therapeutic games can have in promoting mental health (Fagundo et al. 2013; Fernández-Aranda et al. 2012). Specifically, preliminary data suggest that therapeutic games can be effective in reducing emotional difficulties in this age category, especially depressive and anxiety symptoms (Merry et al. 2012; Wijnhoven et al. 2015). However, although previous research emphasized the potential of therapeutic games, little is known about their impact on the underlying biological correlates of emotional difficulties. A particular interest of the present study is the psychophysiological model that links frontal brain asymmetry to individual differences in emotional difficulties.

Frontal alpha asymmetry is a major biological index involved in emotional reactivity, an important process integral to emotional well-being. A highly influential model formulated by Davidson (Davidson et al. 1990; Wheeler et al. 1993) proposes that emotional responding is related to variations in activation of the right and left frontal brain regions. Specifically, this model suggests that greater activity in the right frontal hemisphere is linked to a withdrawal motivational system that is activated when an individual experiences negative emotions and is moving away from threatening situations. Conversely, greater activity in the left frontal hemisphere is associated with an approach motivational system that is activated when an individual experiences positive emotions and is moving towards goals (Davidson 1998). Research has shown that children and adolescents who show right frontal asymmetry are more likely to experience higher negative affect, to be more inhibited, and show increased distress in response to threatening situations (Calkins et al. 1996; Fox et al. 1992; Fox et al. 2001). On the other hand, left frontal asymmetry in children and adolescents has been found to predict increased positive emotions, decreased negative emotions, and better emotion regulation skills (Jackson et al. 2003; Tomarken et al. 1992). Although previous research has found that frontal asymmetry can be modulated following classic therapeutic interventions (e.g., Cognitive-Behavioral Therapy (CBT); Moscovitch et al. 2011; Rabe et al. 2008; Saraladevi 2013), more research is needed to further elucidate whether frontal asymmetry effectively serves as a biological marker of emotional difficulties and whether newly developed psychological interventions for children and adolescents modulate the reactivity of this index. Moreover, to our knowledge, no study to date has investigated patterns of change in frontal asymmetry among children and adolescents before and after a therapeutic video game intervention.

In this context, the *RET*hink online video game was designed to respond to the mentioned gaps in psychological research, aiming to offer an accessible and attractive evidence-based prevention tool that can be used as a stand-alone intervention to promote emotional resilience in children and adolescents, aged between 10 and 16 years. More specifically, our goal was to help this age category to learn rational thinking styles and other emotion regulation skills to effectively cope with negative emotions such as maladaptive fear, sadness, and anger and promote a healthy emotional and physiological reactivity in response to stressful situations. *RET*hink is based on Rational Emotive Behavior Education (REBE) (Trip et al. 2007) derived from Rational Emotive Behavioral Therapy (e.g., Ellis 1995), which focuses on helping people to change their irrational beliefs and thoughts in order to prevent psychopathology and cultivate a rational thinking style, healthy emotions, and happiness.

In the present study, the primary aim was to investigate whether the *RET*hink online video game can be effective in terms of modulating the subjective and psychobiological responses manifested by children and adolescents in the face of an acute social-evaluative stressor (i.e., an impromptu speech task). We hypothesized that the *RET*hink online video game would reduce the acute emotional and physiological reactions manifested in anticipation, during, and after a social-evaluative threat. Specifically, we predicted that relative to a Waitlist condition, our newly developed intervention would dampen the subjective and biological stress responses during the impromptu speech task. In addition, we expected that the *RET*hink group will provide similar results compared to a classical REBE intervention.

Methods

The methodology of this randomized clinical trial is part of a larger project described in detail elsewhere, and only the most important aspects are presented here (David et al.

2018; see also "Efficacy of the *RETh*ink Therapeutic Online Game," trial registration: clinicaltrials.gov, identifier: NCT03308981, https://clinicaltrials.gov/ct2/show/NCT03308981).

Participants

A total number of $N = 165$ healthy children and adolescents, aged between 10 and 16 years, were recruited for the present study on a voluntary basis from two middle schools located in a small urban community. Children and their parents were asked to provide an informed consent to participate in the present study. An a priori estimation of the sample size was conducted to examine the efficacy of the *RETh*ink game in comparison to a Waitlist condition at post-test in order to detect a medium-to-large effect size (Cohen's $d = .60$) (in a two-tailed test), with a type I error probability of $\alpha = .05$ and a statistical power of .80. Given these parameters, we obtained a sample of 45 participants per group (135 participants in total). Considering a dropout rate of up to 20%, the power analysis revealed that the sample size required should be of at least 162 participants. Thus, the current sample size was in the expected range for the comparison mentioned above. Participants were excluded from the present study if they had (1) a limitation that precluded them to use the iPad, (2) a major psychological disorder, or (3) had (in the past 3 months) psychotherapy or psychiatric treatment. Next, subjects were randomly assigned to one of three groups ($N = 56$ in the Waitlist condition, $N = 55$ in the REBE condition, and $N = 54$ in the *RETh*ink condition). Out of the randomized participants, 31 (18.78%) did not complete the initial impromptu speech task, and thus, these subjects were excluded from the analysis and treated as dropouts (19.64% in the Waitlist condition, 23.63% in the REBE condition, and 12.96% in the *RETh*ink condition). The final sample for this phase of the study consists of 134 subjects: 45 in the Waitlist condition, 42 in the REBE group, and 47 in the *RETh*ink group (Fig. 1). The mean age of the participants was 12.96 (SD = 2.17) in the Waitlist condition, 12.81 (SD = 1.92) in the REBE group, and 13.04 (SD = 2.07) in the *RETh*ink group. Also, the sample comprised 41.8% girls and 58.2% boys (see Table 1 for specific demographic characteristics). A permuted block randomization approach was used to ensure balance of the treatment groups with respect to the participants' grade. The study was approved by the Institutional Review Board of Babeș-Bolyai University.

Procedure

Interventions

The *RETh*ink Game *RETh*ink is a therapeutic videogame that can be accessed online through iOS Apps. It was developed to be used as a stand-alone application to promote rational thinking skills and emotional resilience in children and adolescents. RETMAN is the main character of the game, and his mission is to help children and adolescents to develop effective emotion regulation skills in order to better cope with dysfunctional emotions like anxiety, anger, and depression. In his missions, RETMAN has five friends that support him to help people on Earth to be more rational and happier and escape the power of his opponents, Irrationalizer and his evil friends, the root of irrational thinking, dysfunctional negative emotions, and unhappiness in people's lives.

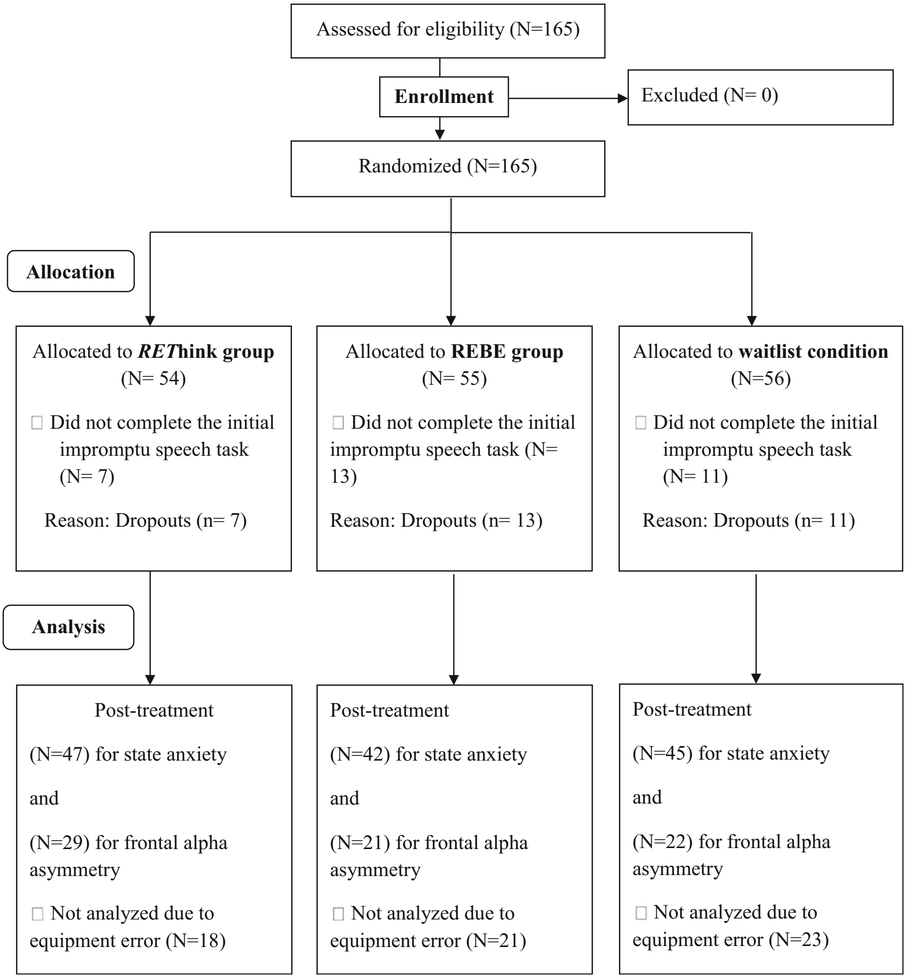

Fig. 1 Flow diagram of the progress through the phases of the trial

The game has seven levels, and each participant played twice each level over 4 consecutive weeks on an Apple iPad Air 2.

Table 1 Demographic characteristics of the participants by group

Sample characteristics	Waitlist ($n = 45$)	REBE ($n = 42$)	*RET*hink ($n = 47$)	Statistical significance (χ^2/F)	p value
Gender, n (%) female, χ^2	21 (46.7)	23 (54.8)	34 (72.3)	6.52	.038
Age range, M (SD), F	10–17	9–16	10–17	.14	.867
	12.96 (2.17)	12.81 (1.92)	13.04 (2.07)		
Pre-adolescents (9–12), n (%)	21 (46.7)	23 (54.8)	21 (44.7)		
Adolescents (13–17), n (%)	24 (53.3)	19 (45.2)	26 (55.3)		

The REBE Group Intervention The REBE group intervention protocol was based on the REBE theory (Ellis 1995) and was delivered in a traditional classroom format. The protocol had the same structure as the *RET*hink protocol (seven modules). The REBE intervention aims to help children and adolescents to develop better emotion regulation skills through promoting a rational thinking style, emotion recognition, and problem solving abilities in order to prevent emotional difficulties (Trip et al. 2007). The seven modules were delivered twice to each participant over 4 consecutive weeks.

The Waitlist The Waitlist group completed only the pre- and post-assessments and will receive the *RET*hink game-based intervention after a 6-month follow-up assessment. This control group served as an untreated comparison group; children and adolescents participated only at the pre-intervention impromptu speech task and again at the post-intervention impromptu speech task.

The Impromptu Speech Task

All participants were asked to complete an impromptu speech task twice, before and after the interventions, while their emotional responses (subjective and physiological) were recorded. Specifically, after they arrived in the experiment room, children and adolescents completed a baseline measure of state anxiety, along with a 3-min baseline recording of frontal brain electrical activity (EEG) while they sit quietly. After the baseline period, participants were informed that they would have to give a 3-min speech in front of a video camera on a controversial topic and that their performance will be evaluated later by a group of experts. Immediately after, children and adolescents were asked to rate their state anxiety having in mind that the speech will come next, followed by a 3-min recording of regional EEG anticipating the speech (i.e., anticipatory anxiety). The topics of speeches included several controversial issues (e.g., Should fast food be banned?) and were randomly delivered across participants. Further, children and adolescents were asked to deliver the 3-min speech on the given subject. Regional EEG was collected continuously during this period. Immediately after the speech, participants were asked to rate how anxious they felt during the speech (i.e., speech anxiety). After a 3-min recovery period, in which participants sat quietly and relaxed while regional EEG was collected continuously, they rated again their levels of anxiety (i.e., recovery anxiety). This procedure was followed by each participant at pre-intervention, as well as post-intervention (Fig. 2). Finally, each participant was debriefed and thanked for participation in the present study. Important to note, in the present study, we selected an impromptu speech task as an emotion induction procedure due to its potential to induce subjective feelings of anxiety in the context of more ecological validity, given that such a performance situation is very common and it represents a core fear in this age category (e.g., Beesdo et al. 2009). The experimental paradigm used in the present study represents an adapted version of the impromptu speech task from the Trier Social Stress Task (Kirschbaum et al. 1993). Previous research consistently showed that this emotion induction procedure is effective in inducing anxiety, thus a valid method to induce such feelings in individuals (Hofmann et al. 2009; Anderson and Hope 2009). Thus, for the purpose of the present study, we considered that this task is adequate in order to induce short-term anxiety in children and adolescents.

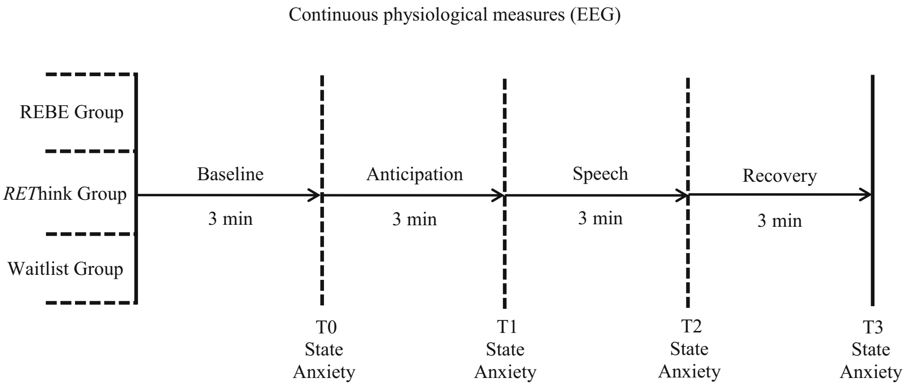

Fig. 2 The impromptu speech task procedure

Dependent Measures

Subjective Anxiety Measurement

The Profile of Affective Distress (PAD) (Opris and Macavei 2007) is a 26-item scale that measures negative emotions within two major categories: "concern and anxiety" and "sadness and depression". In the present study, the "concern and anxiety" subscale was used to measure state anxiety experienced in response to an impromptu speech task. The subscale comprises 12 anxiety-related adjectives (e.g., tense, scared, anxious), and participants were asked to rate on a 5-point Likert scale (1—not at all, 5—extremely) the degree to which they felt the emotion described by the item. Higher scores represent higher state anxiety experienced by participants. They filled this scale after each phase of the impromptu speech task (baseline, anticipation, speech, and recovery). The PAD scale was selected because it was developed and has established psychometric properties on a Romanian speaking population and was successfully used in other studies (Gavița et al. 2012). In the current sample, data indicate good reliability for the anxiety/concern subscale in all phases (α between .85 and .93).

Frontal Alpha Asymmetry Measurement

Data Collection EEG data were recorded using the Emotiv EPOC 14-channel EEG wireless recording headset (Emotiv Systems, Inc., San Francisco, CA). The electrode scheme was arranged according to the international 10–20 system and included active electrodes at AF3, F7, F3, FC5, T7, P7, O1, O2, P8, T8, FC6, F4, F8, and AF4 positions, referenced to the common mode sense (CMS-left mastoid)/driven right leg (DRL-right mastoid) ground. The acquired data were digitized using the embedded 16-bit ADC with 128 Hz sampling frequency per channel and sent to the computer through wireless technology. Prior to using the headset, all felt pads were moistened with a saline solution. During the entire procedure, real-time sensor contact quality was visually monitored by the experimenter to ensure quality of measurements. Also, the markers were manually set according to each phase of the experiment.

Pre-processing Steps and Analysis Raw data have been pre-processed and analyzed in EEGLab and Brainstorm. Continuous recordings were high-pass filtered (0.5 Hz) and segmented into 2-s non-overlapping epochs between the markers. Epochs with activity in any channel with amplitude greater than ± 1000 μV were excluded in order to remove gross artifacts. Then ICA was applied on the remaining epochs, and the components related to eye artifacts were removed. Cleaned epochs with activity greater than ± 100 μV were further rejected in order to remove those epochs that still contained artifacts. The resulting pre-processed epochs (an average of 67% per participant) were analyzed with FFT in order to derive the spectral activity in the alpha band (range 8–13 Hz) for each Time (pre-intervention and post-intervention), Phase (baseline, anticipation, speech, and recovery), and Group (Waitlist vs. REBE vs. *RETh*ink). Frontal alpha asymmetry index was calculated according to the formula log (Alpha Right Electrode) − log (Alpha Left Electrode). One pair has been considered for analysis of fontal alpha asymmetry index, F7-F8 pair located in the frontal region. Higher scores represent that it is more alpha at the right site compared to the left site, meaning that the right hemisphere, which is related to withdrawing motivation and negative affect, is more inhibited. The EEG data were analyzed only for 72 participants due to equipment error ($N = 22$ in the Waitlist condition, $N = 21$ in the REBE condition, and $N = 29$ in the *RETh*ink condition).

Statistical Analysis

To analyze the data on state anxiety, we used repeated measures ANOVA with time of measurement (pre-intervention vs. post-intervention) and phase of the impromptu speech task (before vs. anticipation vs. speech vs. recovery) as the within-subjects factors and the groups of treatment (Waitlist vs. REBE vs. *RETh*ink) as the between-subjects factor. Significant main effects and the interaction effects were further explored using Sidak adjusted pairwise comparisons of estimated marginal mean. As an indicator of effect size for the main and the interaction effects, we computed η_p^2 while Cohen's d index was selected for significant pairwise comparisons.

Further, to analyze the data on frontal alpha asymmetry, we used a mixed-model approach, which is a relatively novel approach that extends the classical linear model (i.e., the one behind linear regression and ANOVA models) and is more suitable in physiology research. Very briefly, mixed models have the advantage to use random factors that allow modeling the non-independence of the observation more effectively compared to repeated measures ANOVA. Also, very importantly, they have the advantage to use all the data even if there are missing observations (Bagiella et al. 2000; Boisgontier and Cheval 2016). This is the case for the present study, in which outlier observations, defined as those observations falling below Q1 − 1.5*IQR and observations falling above Q3 + 1.5*IQR (where Q1 and Q3 stands for first and third quartile and IQR for inter-quartile range), were removed before fitting the model. This approach resulted in having, for some participants, an incomplete set of observations, which would be entirely removed using standard rm-ANOVA. The resulting F-test performed to assess the significance of the fixed effects (Time, Phase, and Group) was performed using the Satterthwaite approximation for computing the denominator degrees of freedom (Luke 2017; Maffei et al. 2019).

Finally, in order to directly assess the relationship between EEG alpha frontal asymmetry and self-reported anxiety scores, we performed a correlation analysis between asymmetry scores and the anxiety/concern subscale of PAD collapsed across the task phases. The reported p values have been corrected for the multiple comparison problem using Benjamini and Hochberg's procedure to control the false discovery rate Benjamini and Hochberg 1995. All the analyses for frontal alpha asymmetry have been performed in R, using the packages Ime4, ImerTest, and Ismeans.

Results

Descriptive statistics for all measures are presented in Table 2.

For the main analysis on state anxiety, we identified a significant within-subjects effect of Time (pre-intervention vs. post-intervention), F (1, 131) = 12.861, $p < .001$, $\eta_p^2 = .08$ (scores have decreased across the full sample), as well as a significant within-subjects effect of Phase (baseline vs. anticipation vs. speech vs. recovery), F (1.92, 251.79) = 190.205, $p < .001$, $\eta_p^2 = .59$, but no significant between-subjects effect of Group was found (Waitlist vs. REBE vs. *RET*hink), F (2, 131) = .23, $p = .790$. With respect to the within-subjects effect of Phase, simple contrasts showed that state anxiety has increased globally from baseline to anticipation, F (1, 131) = 155.093, $p < .001$, $\eta_p^2 = .54$, and from baseline to speech, F (1, 131) = 229.866, $p < .001$, $\eta_p^2 = .63$, but not from baseline to recovery ($p > .05$). Next, in order to have a better understanding of the results, we looked at the interaction effects. We found a significant Time × Phase interaction, F (2.593, 339.693) = 12.648, $p < .001$, $\eta_p^2 = .08$. No other interaction effects were found for state anxiety (p values > .05). We further computed pairwise comparisons, and the results pointed out that the Time × Phase interaction effect was explained by a decrease from pre- to post-intervention in state anxiety scores for speech ($p < .001$, $d = .43$) and recovery phase ($p < .001$, $d = .25$), but not for baseline ($p > .05$) and anticipation ($p = .061$). Also, we compared the evolution of scores within the four phases at pre-intervention and post-intervention, and a similar pattern was observed at both times. State anxiety has significantly increased from baseline to anticipation, from anticipation to speech, and from speech to recovery ($p < .001$ for all comparisons between phases at both times), but have not significantly changed from baseline to recovery ($p > .05$ at both times). Thus, the emotion induction proved to be effective in inducing anxiety, as well as the recovery period in helping participants to return to similar levels of anxiety as those experienced during the baseline period (see Table 2, Fig. 3).

For the main analysis on frontal alpha asymmetry, we identified a significant within-subjects effect of Time (pre-intervention vs. post-intervention), F (1, 558.90) = 6.12, $p < .001$, but no significant within-subjects effect of Phase (baseline vs. anticipation vs. speech vs. recovery), F (4, 552.50) = .19, $p = .942$, as well as no significant between-subjects effect of Group (Waitlist vs. REBE vs. *RET*hink), F (2, 65.50) = .23, $p = .791$. Further, we found a significant Time × Group interaction, F (2, 558.54) = 13.88, $p < .001$ (see Supplementary Table 1 for more details). No other interaction effects were found for frontal alpha asymmetry (p values > .05). Pairwise comparisons showed that the Time × Group interaction effect was explained by an increase from pre- to post-intervention in frontal alpha asymmetry scores specific for the *RET*hink group ($p < .001$, $d = .69$; see Fig. 4).

Table 2 Descriptive statistics: means and SD on all variables

	Waitlist		*RET*hink		REBE	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Baseline anxiety	5.44 (4.48)	5.00 (5.23)	4.65 (4.83)	5.80 (6.80)	5.61 (6.03)	6.45 (7.10)
Anticipatory anxiety	11.24 (6.72)	9.24 (8.26)	11.21 (9.05)	10.31 (10.23)	12.02 (10.60)	10.71 (10.10)
Speech anxiety	18.86 (11.41)	14.84 (11.73)	21.10 (12.18)	16.04 (13.53)	19.23 (13.22)	14.61 (12.42)
Recovery anxiety	4.84 (6.46)	4.46 (5.79)	8.48 (9.92)	4.19 (7.63)	4.30 (5.76)	4.85 (5.55)
Baseline FAA	0.88 (0.48)	1.05 (0.46)	0.77 (0.72)	1.12 (0.60)	0.94 (0.52)	0.90 (0.51)
Anticipatory FAA	0.85 (0.45)	0.92 (0.33)	0.78 (0.60)	1.12 (0.58)	0.95 (0.56)	1.03 (0.64)
Speech FAA	0.79 (0.46)	0.97 (0.50)	0.77 (0.60)	1.05 (0.60)	1.14 (0.79)	0.86 (0.55)
Recovery FAA	0.95 (0.65)	1.01 (0.48)	0.82 (0.65)	1.05 (0.61)	0.92 (0.51)	0.94 (0.59)

Standard deviations (SD) are presented between brackets

FAA frontal alpha asymmetry

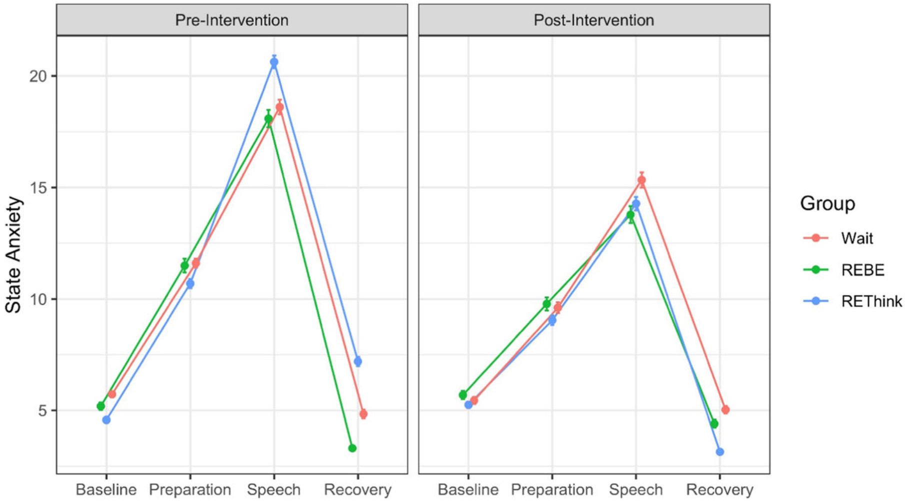

Fig. 3 Graphical representation for changes in state anxiety during the impromptu speech task at pre- and post-intervention

Finally, for what concerns the relationship between electrophysiological and self-reported measures, the correlation analysis between frontal alpha asymmetry and state anxiety measured in the three groups before and after the interventions revealed a significant negative relationship after the *REThink* intervention ($r_{(105)} = -.39$, $p_{\text{fdr-corrected}} < .0001$). No significant associations were observed in the other two groups (Fig. 5, Table 3).

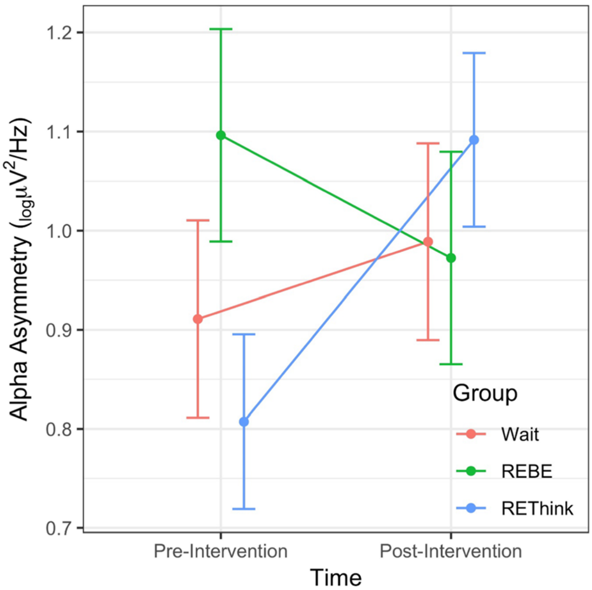

Fig. 4 Graphical representation for changes from pre- to post-intervention in frontal alpha asymmetry

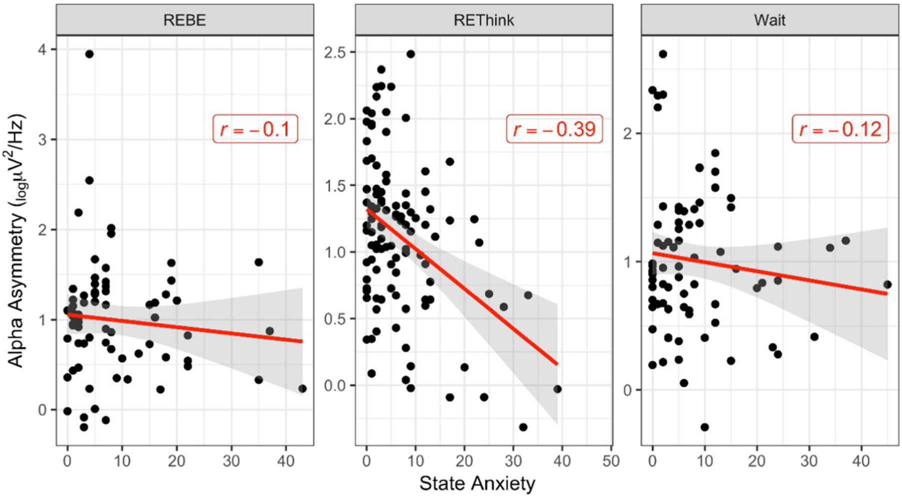

Fig. 5 Graphical representation for the associations between frontal alpha asymmetry and state anxiety measured in the three groups after the interventions

Discussion

The present study investigated the efficacy of the *RETh*ink therapeutic online game in modulating psychobiological responses manifested by children and adolescents in the face of an acute social-evaluative stressor. Specifically, we expected that relative to a Waitlist condition, the *RETh*ink game will reduce state anxiety and increase frontal alpha asymmetry during a stressful task. Also, we predicted that the *RETh*ink group will provide similar results for these indexes compared to a classical REBE intervention.

Our results showed that state anxiety significantly decreased from pre- to post-intervention, but contrary to our expectations, this reduction was irrespective of group. Scores have decreased in all three conditions (Waitlist vs. REBE vs. *RETh*ink), which in fact might reflect a habituation effect that occurred for children and adolescents from the first application of the impromptu speech task to the second one. Moreover, results

Table 3 Correlation analysis between frontal alpha asymmetry and state anxiety measured in the three groups before and after the interventions

Time	Group	Correlation	*df*	$p_{\text{fdr-corrected}}$
Pre-intervention	REBE	− .02	72	.83
	*RETh*ink	− .11	101	.39
	Waitlist	.23	73	.14
Post-intervention	REBE	− .1	66	.41
	*RETh*ink	− .39	105	< .0001
	Waitlist	− .12	76	.41

df degrees of freedom, $p_{\text{fdr-corrected}}$ *p* values corrected for multiple comparison using Benjamini and Hochberg's procedure (Benjamini and Hochberg 1995) pointed out that this decrease in state anxiety from pre- to post-intervention was specific to the speech and recovery phases, but not significant in the baseline and anticipation phases.

With respect to the biological index, results revealed a significant increase in frontal alpha asymmetry from pre- to post-intervention; further analysis showed that this increase was specific for the *RETh*ink group only, meaning that the frontal areas of the right hemisphere, which are related to withdrawing motivation and negative affect, were more inhibited in this group after the intervention. Such a result provides support for the efficacy of the *RETh*ink online intervention in reducing the modulation of one of the most known psychophysiological correlate of negative emotions/withdrawing motivation in children and adolescents in the face of social-evaluative stress, in line with previous adult studies that already showed the efficacy of non-pharmacological clinical intervention in modulating frontal alpha activity (Moscovitch et al. 2011; Rabe et al. 2008; Saraladevi 2013). Also, this result is somewhat surprising because it shows that this newly developed intervention has a greater effect on frontal alpha asymmetry not only compared to a Waitlist condition but also compared to a classical REBE intervention. This lack of findings on the efficacy of REBE intervention contradicts past research which demonstrated its efficacy (Trip et al. 2007) and also contradicts studies which showed that frontal alpha asymmetry can be modulated following classic therapeutic interventions (Moscovitch et al. 2011; Rabe et al. 2008; Saraladevi 2013). A possible explanation for this result might be that (1) REBE was delivered before in these schools by their school psychologist and (2) REBE in the present study was delivered in a traditional classroom format, which might have diminished its beneficial impact, especially on physiological indexes. At the same time, this highlights the potential of therapeutic video games which offer a more personalized and engaging interaction with the user that may benefit the efficacy of the intervention, with lasting effects even at a biological level (Fleming et al. 2017).

Another interesting result of the present study showed that increases in frontal alpha asymmetry from pre- to post-intervention for the *RETh*ink group were not characteristic to a specific phase of the task (baseline vs. anticipation vs. speech vs. recovery). In particular, scores increased from pre- to post-intervention irrespective of the phase of task. This suggests that frontal alpha asymmetry should be treated more as a trait psychophysiological index, meaning that it is best conceived as an indicator of the tonic affective state rather than a phasic indicator, explaining why there is no evidence for differences across the phases of the speech task (for a review of trait vs. phasic nature of frontal alpha asymmetry see Coan and Allen 2004 and Reznik and Allen 2018).

Overall, the present results suggest that the *RETh*ink therapeutic video game is effective in modulating the frontal brain activation manifested by children and adolescents in response to an impromptu speech task, but not for reducing subjective state anxiety. However, the significant effects only for frontal alpha asymmetry and not for subjective anxiety are not unusual. Research pointed out that it is common to find dissociation between different response domains (self-report vs. physiological; Mauss and Robinson 2009). This dissociation might be explained on the one hand by the fact that self-report measures are a more explicit indicator of affect, requiring the use of (meta)cognitive strategies to have an insight over subjective states, which is particularly challenging for children (Deighton et al. 2014). On the other hand, physiological indexes are more objective and implicit measures, as well as more insensitive to cognitive and social factors that bias self-report, and thus allow probing of emotional response with a relatively less unbiased measure (Reis and Judd 2000). Moreover, the observed negative relationship between frontal asymmetry and reported anxiety after the *RET*hink intervention clears the field from the possibility that the two measures are tapping into distinct processes. Instead, it provides support for the theoretical model that sees frontal alpha asymmetry as a neural correlate of emotions and motivation while showing that the relationship between the two domains (physiological and psychological) is complex and still hard to define clearly.

Our findings are in line with recent research on technology-based interventions, providing support for the beneficial effects of therapeutic video games in improving emotional resilience and promoting mental health in children and adolescents (Merry et al. 2012). In addition, our results extend previous findings offering a more nuanced perspective on investigated outcomes by following changes in physiological indexes that occurred after the therapeutic video game intervention. To our knowledge, this is the first study to investigate patterns of change in frontal alpha asymmetry among children and adolescents before and after a therapeutic video game intervention. This study offers important preliminary data regarding the efficacy of the *RET*hink therapeutic video game in modulating psychobiological responses manifested by children and adolescents in the face of social-evaluative threat. However, more studies are necessary for documenting these effects using multiple physiological indexes (e.g., heart rate variability, skin conductance, respiratory sinus arrhythmia, cortisol level). The present study was limited to a convenience sample from two middle schools located in a small urban community, thus limiting the generalizability of the present findings. Future research should include more diverse samples and continue to provide a more nuanced perspective on the investigated outcomes, not limited to subjective aspects. Moreover, it is important to consider that the present research suffered from participant dropout due to the inherent limitation of the equipment used, which led us to consider in the EEG analysis just a subset of the total sample. Future studies will aim at replicating the current EEG results in a larger sample to bolster the claim for the efficacy of the *RET*hink intervention in modulating frontal alpha asymmetry. Moreover, future studies should aim at replicating the current findings with the use of standard recording equipment in order to improve the quality of the recorded signals. Indeed, the great usability of wireless EEG recording system comes with the cost of a relatively poorer SNR of the data, compared to standard equipment, since wireless systems dramatically improve the participant's comfort, which leads to a larger amount of movements that unfortunately impacts the quality of the data. The use of standard EEG recording systems in future studies will lead to relaxing the very stringent preprocessing and statistical criteria adopted in the current study and provide a better quantification of the psychophysiological processes involved in mediating the relationship between therapeutic interventions and individual emotional state. An important limitation is that the anxiety subscale of the PAD has not been validated in children and adolescent samples, and thus, this limitation could explain why we did not find changes regarding subjective variables; future studies should employ measures specifically designed for children and adolescents in measuring emotions. Another important limitation is the lack of control on the level of metacognitive insight for children and adolescents when they filled out the subjective measures. Future studies could highlight important results that past research has omitted due to lack of control over participants' insight in filling out subjective measures.

In conclusion, current findings provide further evidence suggesting that therapeutic video games adapted for tablets and smartphones are indeed a useful tool in improving mental health in children and adolescents, with an impact up to the physiological level. Finally, we suggest that bridging together the attractiveness of video games and the accessibility of mobile phones and tablets with the principles from well-supported psychological interventions will pave the way for more innovative and efficacious psychological interventions.

Compliance with Ethical Standards

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