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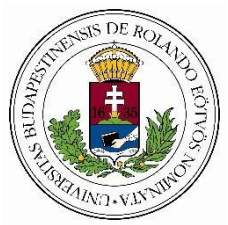

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PSYCHOLOGICAL AND BIOLOGICAL CORRELATES OF PERSEVERATIVE COGNITIONS

THESES OF THE DOCTORAL DISSERTATION

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1. Background and aims

The aim of our work was to provide new insights into the interpretation of perseverative cognitions, especially rumination. Rumination is often defined as a passive and repetitive thinking process, which focuses one's attention to depressive symptoms and to reasons and consequences of these symptoms; so in this framework rumination is conceptualized as a possible response to depressed mood (Nolen-Hoeksema, 1991). Accumulated evidence indicates that rumination plays an important role in the development and maintenance of mood and anxiety disorders (Aldao, Nolen-Hoeksema, & Schweizer, 2010; McLaughlin & Nolen-Hoeksema, 2011; Nolen-Hoeksema, 2000), highlighting the importance of those intervention techniques, which actively target rumination. Rumination-focused interventions are especially important in the treatment of therapy-resistant depression and in the prevention of comorbid disorders (Nolen-Hoeksema & Watkins, 2011; Watkins et al., 2007). In addition, rumination and worry (a construct, correlating highly with rumination) are also thought to contribute to externalizing psychopathology and somatic health, hence they could be defined as transdiagnostic intrapersonal characteristics (Hsu et al., 2015; Nolen-Hoeksema, Stice, Wade, & Bohon, 2007; Ottaviani et al., 2016).

Perseverative cognitions however are not an exclusive feature of clinical populations and they can be present in individuals with healthy psychological functioning (Papageorgiou & Wells, 2004; Wells & Matthews, 1996). Rumination is believed to be a normal process which facilitates self-regulation and helps problem solving (Grossmann & Kross, 2010; Harrington & Loffredo, 2011; Lyubomirsky, Layous, Chancellor, & Nelson, 2015), therefore, it is essential to identify those associations and underlying mechanisms by which this adaptive process becomes maladaptive and creates a risk for development of disorders.

The early mapping of ruminative and worrying thoughts (also known as nonproductive thoughts) is especially important among *children and adolescents*, so that preventive efforts can work toward the avoidance of subsequent mental disorders and somatic health complaints. Furthermore, the investigation of *gender differences* in rumination/worry is meaningful from both theoretical and therapeutic considerations. Although girls tend to ruminate more than boys (Aldao et al., 2010), findings of several meta-analysis show that the effect sizes of the gender differences are small (even negligible) (Johnson & Whisman, 2013; Rood, Roelofs, Bögels, Nolen-Hoeksema, & Schouten, 2009; Tamres, Janicki, & Helgeson, 2002).

For this reason, reliable and valid instruments are needed to explore whether true gender differences exist in rumination. Many questionnaire studies do not examine if the different answers reflect true gender differences or just an artefact because the groups interpret the scale items differently (Milfont & Fischer, 2010). Consequently, testing *gender invariance* of a scale is a prerequisite of interpreting any group differences, which is particularly important in relation to rumination and worry. However, only few studies tested measurement invariance of scales designed specifically for children and adolescents (Carter et al., 2010; Cox et al., 2011).

In light of the above mentioned theories, the **I. research question** of the dissertation is:

> **I:** Whether the *Nonproductive Thoughts Questionnaire for Children (NPTQ-C)* (Jellesma, Terwogt, Reijntjes, Rieffe, & Stegge, 2005) is a reliable instrument for adolescents that also shows gender invariance.
> Two different studies were conducted to answer this question.

1) In our first study, the factor structure, gender invariance, reliability and convergent validity of NPTQ-C were tested in a representative sample of adolescents (N=1572).

2) In our second study, we aimed to test the construct validity of the scale in a smaller sample of school-aged youth (N=385).

In addition, it is worthwhile to investigate gender differences in the relationship of rumination and mental/somatic health to get a deeper understanding about its complex associations. For instance, it remains to be seen whether ruminating boys experience more somatic symptoms than ruminating girls, and whether age is a significant moderator. The invariance of the relationship between rumination/worry and the positive aspects of psychological functioning is also unclear (Jellesma, 2008; Nolen-Hoeksema & Jackson, 2001).

Based on the above our **II. research question** is:

> **II**: Do nonproductive thoughts (trait rumination and trait worry) significantly influence mental well-being and somatic symptoms of healthy adolescents? Do gender and age significantly moderate the *strengths of these relationships*?
> Empirical testing of the questions was based on the dataset gathered in our first study (N=1572).

Although rumination is often discussed as a past-oriented thinking process which is mainly related to the processing of negative (emotional) stimuli (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), recent theories suggest that rumination could influence the ***anticipation*** processes as well, and it is a risk factor in many pathologies (eg. depression, substance use, eating disorder etc.) where the ***reward processing*** is altered (Nolen-Hoeksema et al., 2007; Watkins, Grafton, Weinstein, & MacLeod, 2015). Previous studies with depressed or remitted depressed patients showed (Schiller et al., 2013), that rumination may influence the neural responses yielded for the cues indicating reward or punishment. However, it remains unclear whether the results could be attributed to depression and whether trait rumination relates to the neural responses during the anticipation of putative reward/loss cues or the consumption of rewarding/punishing outcomes.

Therefore, our **III. research question is**:

> **III:** Whether trait rumination could be significantly associated with neural responses during (secondary) reward/loss anticipation and consumption.

3) This question was tested in a functional magnetic resonance imaging (fMRI) study among healthy (never depressed) adults (N=37).

Previous findings indicate that the elevated level of trait rumination is associated with psychological inflexibility, which could be reflected in different biological indices as well (Thayer et al., 2012). The *resting heart rate variability (HRV),* as a physiological index of the inflexible adaptation to environmental demands, is consequently reduced in relation to trait rumination and trait worry (Ottaviani et al., 2016; Visted et al., 2017; Williams et al., 2015, 2017). Still several unanswered questions remain in the literature. One of them is that the majority of the studies refer to rumination as a unidimensional construct and do not measure its maladaptive (brooding) and adaptive (reflection) facets. In addition, it is unknown whether dispositional or state rumination /worry have more influence on resting HRV, however in a meta-analysis, Ottaviani and colleagues (2016) found that only state perseverative cognitions

showed significant negative associations with this construct. Furthermore, perseverative cognitions have only been measured in experimental studies where rumination or worry have been induced, and no study has assessed state perseverative cognitions during resting HRV registration, although previous neuroimaging studies shed light on the importance of measuring self-reported intrusive thoughts during resting state fMRI (Diaz et al., 2013). Kühn and colleagues (2013, 2014) in their fMRI studies also found significant associations between intrusive (unwanted) thoughts and the activity of the fronto-striatal network.

In light of the above, our **IV. research question** is:

IV: Do trait perseverative cognitions and spontaneously occurring (not induced) state ruminative thoughts relate to resting HRV among young adults?

4) In our fourth study we tested the associations of resting HRV, trait rumination, trait worry and state ruminative (intrusive) thoughts among healthy adults (N=130),
5) In our fifth study, we aimed to replicate the results of study 4, and we wanted to test the complex associations between the facets of trait rumination (i.e. brooding, reflective pondering), trait worry and state intrusive thoughts during resting (N=72).

2. Empirical studies

2.1. I. research question (Study I/1): Testing factor structure, gender invariance and validity of the Nonproductive Thoughts Questionnaire for Children (NPTQ-C)[1]

2.1.1. Methods

Data were collected from every primary and high school students in one of the largest districts of Budapest (Csepel). All schools in the district (14 primary schools and 7 high schools) agreed to participate. From each school half of the parallel classes (6-13. grades) were randomly selected. Adolescents completed the questionnaires in their classroom within one class session (45 minutes), where no teaching staffs were present. The sample characteristics therefore reflect the composition of participating classes.

141 parents refused permission and 178 students were absent during data collection. Altogether 1625 youth completed the questionnaires, however, 53 were excluded from the analysis due to missing data. The final representative sample comprised 1572 students (770 boys (49%); mean age=15.39; SD=2.26 years).

Ruminative and worrying thoughts were measured by the NPTQ-C (Jellesma et al., 2005). The one-factor scale consists of 10 items (such as "I am often worried") and participants had to indicate on a 3-point scale (*1= not true, 2=sometimes true, 3=often true*) how often the items apply to themselves. The questionnaire was translated from Dutch to Hungarian by Kökönyei and coworkers with the permission of the original authors. The Hungarian version was back-translated by two independent translators and the final version of the questionnaire was approved by Jellesma.

Besides basic demographic questionnaires, we measured psychological symptoms by the self-reported, Hungarian adaptation of Strength and Difficulties Questionnaire (SDQ)

[1] The present chapter is the copy of the following paper: Kocsel, N., Mónok, K., Szabó, E., Morgan, A., Reinhardt, M., Urbán, R., Demetrovics, Zs. & Kökönyei, Gy. (2017). Gender Invariance and Psychometric Properties of the Nonproductive Thoughts Questionnaire for Children. *Assessment*, 107319111770614.

(Goodman, Meltzer, & Bailey, 1998; SDQ-Magy; Turi et al., 2013). In addition, we used the Big Five Questionnaire for Children to assess personality traits (Barbaranelli, Caprara, Rabasca, & Pastorelli, 2003; Rózsa, 2005).

2.1.2. Main results

The general CFA model indicated good fit to the data ($\chi2$=169.977; df=35; p=0.0001; CFI=.977; TLI= .970; RMSEA= .050). Although the examination of the modification indices revealed that the degree of fit could be increased if correlations of error variances were allowed: between items 5 and 7 and between items 8 and 10. Allowance for the aforementioned correlations improved the degree of fit ($\chi2$=85.156; df=33; p=0.0001; CFI=0.991; TLI= 0.988; RMSEA=0.032) of the indices.

In order to determine whether the factor structure, factor loadings and thresholds of the NPTQ-C are valid in both gender groups we tested invariances (Table 1). According to $\Delta\chi^2$ statistics, the questionnaire does not show metric and scalar level invariance, but several authors argue that the hypothesized invariance should only be rejected if there is a decrease of .01 or larger in CFI and/or if there is a decrease of 0.015 or larger in RMSEA (Cheung & Rensvold, 2002; Dimitrov, 2010). Our results show that the ΔCFI is -0.002 in the metric and <0.001 in the scalar model and that the degree of the decrease does not exceed .01. Similarly, ΔRMSEA is below 0.015. Consequently, based on these fit indices there is evidence of configural, metric, and scalar invariance of NPTQ-C across both gender groups.

Table 1- Testing measurement invariance of Nonproductive Thoughts Questionnaire for Children

	χ^2	df	RMSEA	CFI	*Δχ²*	*Δdf*	*p*	*ΔRMSEA*	*ΔCFI*
CFA in each group separately									
Girls	74.305	33	0.040	0.978					
Boys	58.179	33	0.032	0.990					
Multigroup analyses to test the measurement invariance									
Configural invariance	129.150	66	0.035	0.985	-	-	<0.001		
Configural versus Metric invariance					28.879	9	<0.001	-0.001	-0.002
Metric invariance	144.775	75	0.034	0.983	15.625	9	<0.001		
Metric versus Scalar invariance					18.553	9	<0.05	-0.001	<0.001
Scalar invariance	154.759	84	0.033	0.983	9.984	9	<0.05		

CFA=confirmatory factor analysis; χ^2= Chi-squared test; df= degree of freedom; RMSEA=root mean squared error of approximation; CFI=comparative fit index; Δχ²= χ²difference test calculated with DIFFTEST procedure.

The internal consistency of the NPTQ-C was good (Cronbach's $\alpha = 0.83$), similar to the original version. To eliminate the errors in the estimation of reliability, the omega coefficient was also determined. This also indicated good internal consistency ($\Omega_{total}=0.85$).

In order to measure convergent validity, we applied a MIMIC model, so we could determine the effect of each observed variable on the latent variable while controlling for the effect of other variables. The emotional symptoms factor of the SDQ ($\beta=0.464$, $p<0.001$) and the emotional instability factor of the BFQ-C ($\beta=0.364$; $p<0.001$) showed the strongest positive relation with the NPTQ-C. The conduct problems factor of SDQ ($\beta=-0.118$; $p<0.05$) and energy factor of BFQ-C ($\beta=-0.147$; $p<0.01$) also had a significant but weak negative effect on the ruminative/worrying thoughts.

2.1.3. Discussion

In our first study, we tested the psychometric properties of the Nonproductive Thoughts Questionnaire for Children (NPTQ-C) in a representative sample of healthy adolescents. The confirmatory factor analysis supported the originally proposed one factor structure of NPTQ-C (Jellesma et al., 2005), showing good fit to our data.

In addition, NPTQ-C showed configural, metric and scalar-level invariances across both gender groups, indicating that NPTQ-C is a reliable instrument, which is not substantially affected by gender bias. Our results seem to concord with Carter's (2010) research who found evidence of configural gender invariance of five instruments specifically related to worry and rumination, although these conclusions were solely based on chi-square differences, and confined to adult samples (Carter, 2010; Carter & Bates, 2013). Further studies are needed to clarify whether questionnaires measuring rumination and worry show metric or scalar gender invariance by other indices (e.g., CFI), and whether these observations are valid in adolescence and in childhood.

In terms of internal consistency, the NPTQ-C shows convincing results. Both coefficients (alpha and omega) support the reliability of the scale, which is in line with other studies where the internal consistency of NPTQ-C also proved to be good (Jellesma et al., 2005; Rieffe et al., 2007).

Convergent validity of NPTQ-C was explored using the MIMIC model, and as expected, significant relationship was found with the emotional symptoms factor of SDQ and emotional instability factor of BFQ-C. According to these results, ruminative and worrying thoughts are associated with certain emotional symptoms such as nervousness or dysphoric mood, and with feelings of anxiety, depression, discontent or anger. These results are in line with previous studies, emphasizing the link of rumination and worry to internalizing disorders (Aldao et al., 2010), and to some personality traits such as neuroticism (Roelofs et al., 2008).

2.2. I. research question (Study I/2): Testing construct validity of the Nonproductive Thoughts Questionnaire for Children (NPTQ-C)

2.2.1. Methods

In this study, adolescents were recruited from 12 Hungarian high schools by a convenience sampling method. The procedure for this study was similar to Study I/1: Participants completed self-rated questionnaires in the classroom within one class session on the theme of mental and somatic health. Altogether 397 youth completed the questionnaires, however, 12 were excluded from the analysis due to missing data. The final sample comprised 385 students (131 boys (34%); mean age=16.05; SD=1.23 years).

Besides basic demographic characteristics, we measured nonproductive thoughts by NPTQ-C and trait rumination by the 10-item Ruminative Response Scale (RRS) (Nolen-Hoeksema et al., 1999). This questionnaire assess the different facets of rumination (5-5 items), the

maladaptive brooding and the adaptive reflective pondering (or reflection) (Treynor et al., 2003).

2.2.2. Main results and discussion

We applied a MIMIC model to test the construct validity of the NPTQ-C. We defined the nonproductive thoughts as a latent variable and we investigated the effects of brooding and reflective pondering subscales of RRS on NPTQ-C. In the effects of age and gender were controlled for. While the reflective pondering factor showed significant but weak relationship (β=0.101; $p<0.05$) with ruminative/worrying thoughts, the brooding factor showed strong positive (β=0.643; $p<0.001$) association with NPTQ-C. These findings are completely in line with our previous expectations, and enhance that the nature of thoughts NPTQ-C measures is rather nonproductive and maladaptive than constructive.

In general, our findings show that NPTQ-C is an adequate tool for assessing maladaptive thoughts in adolescent populations. It has good psychometric properties and shows measurement invariance therefore, it is applicable to detect any gender differences that might exist.

2.3. II. research question (Study II/1): Testing the associations of nonproductive thoughts, somatic symptoms and well-being: The moderator role of age and gender[2]

2.3.1. Methods

This study used the same dataset as Study I/1 (N=1572) (see above for the description of the sample and procedure). Based on previous results, we expected to find a significant positive association between rumination/worry and somatic complaints (Jellesma, 2008; Kökönyei et al., 2015; Ottaviani et al., 2016) and negative association between perseverative cognitions and psychological, emotional and social mental well-being (Ciarrochi & Scott, 2006; Harrington & Loffredo, 2011). We also aimed to explore whether the strength of these relationships is significantly moderated by age and gender. According to previous results (Krause et al., 2018; Nolen-Hoeksema et al., 1999; Padilla Paredes & Calvete Zumalde, 2015) we hypothesized a female predominance, namely that the relationship between maladaptive thoughts and somatic/mental health would be stronger among adolescent girls than in boys.

Somatic symptoms (covering the last 2 weeks) were assessed by Somatic Complaints List (SCL; Jellesma, Rieffe, & Terwogt, 2007), the emotional, psychological and social dimensions of well-being were assessed by the Mental Health Continuum Short Form (MHC-SF; Keyes, 2002; Reinhardt, Horváth, Morgan & Kökönyei, 2019).

2.3.1. Main results

A multiple group SEM was performed to examine the effect of nonproductive thoughts on somatic symptoms, and emotional, psychological and social well-being. For the latent variable of somatic symptoms, error covariance was allowed between Item 4 and Item 7. Based on modification indices related to nonproductive thoughts, error covariance was also allowed

[2] The present chapter is the copy of the following manuscript currently under review: Kocsel, N., Horváth, Zs., Reinhardt, M., Szabó, E. & Kökönyei, Gy. (2019). Nonproductive thoughts, somatic symptoms and well-being in adolescence: The moderator role of age and gender. *Under review.*

between Item 5 and Item 7 and between Item 8 and Item 10. The unconstraint model showed acceptable model fit (see Table 2).

Table 2- Testing invariance across age- and gender based groups in the relationship form Nonproductive Thoughts to Somatic Symptoms, Emotional -, Psychological - and Social Well-being

	$\chi 2$	df	RMSEA	CFI	TLI	Wald-Test	p
Unconstrained model	1470.582	547	0.033	0.937	0.931		
Assuming equality between the relationship of NPTQ-C and SCL, EWB, PWB, SWB across groups	3417.628	2575	0.029	0.927	0.933		
NPTQ-C – SCL						11.176	0.011
NPTQ-C – EWB						4.578	0.206
NPTQ-C – PWB						4.944	0.176
NPTQ-C – SWB						4.670	0.198

Groups: (1) Boys between the age of 11 and 14; (2) Girls between the age of 11 and 14; (3) Boys between the age of 15 and 20; (4) Girls between the age of 15 and 20. NPTQ-C = Nonproductive Thoughts Questionnaire for Children, SCL = Somatic Complaint List, EWB = Emotional Well-being, PWB = Psychological Well-being, SWB = Social Well-being; χ^2 = Chi Square test statistics; RMSEA = Root Mean Squared Error of Approximation; CFI = Comparative Fit Index; TLI = Tucker-Lewis Index; Chi Square test statistics are significant at least p < .001 level.

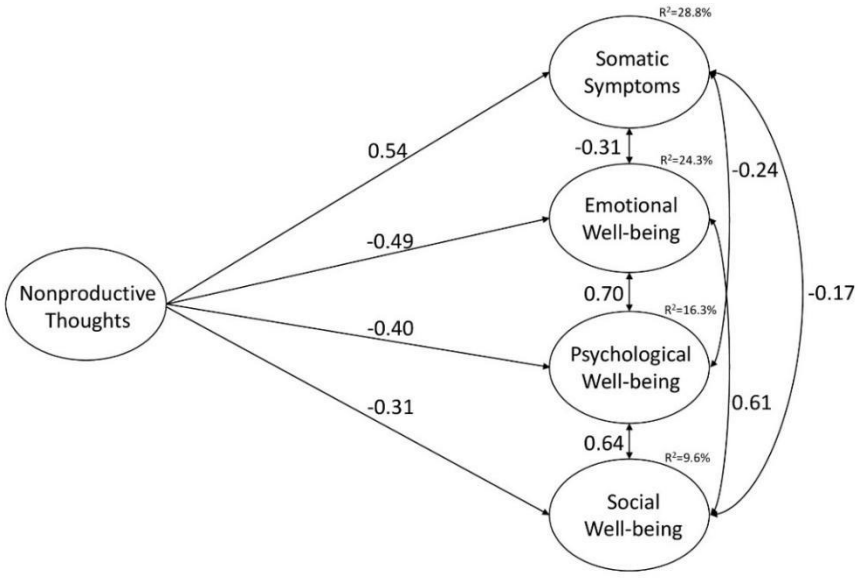

Figure 1. Relationship between nonproductive thoughts, somatic Symptoms and mental well-being

Figure 1 illustrates the relationships between the independent and dependent latent variables. Higher rates of nonproductive thoughts predicted an elevated level of somatic symptoms, while nonproductive thoughts had a negative relationship with each of the well-being factors.

In the next stage of the analysis, the invariance of the regression path coefficients were tested across four groups. Based on the research of Arnold (2014) and Hankin (2009) we decided to split the sample at the age of 14, since the onset of psychopathologies was associated with this critical time of adolescence, and this age also overlapped with major social and educational changes in the lives of our participants (transition from elementary to high school). The participating adolescents were divided into four groups: (1) boys between the ages of 11 and 14; (2) girls between the ages of 11 and 14, (3) boys between the ages of 15 and 20, and (4) girls between the ages of 15 and 20. Again, invariance was accepted if the change in the value of CFI and RMSEA was below or equal .010 and .015 (Chen, 2007).

The Wald test was calculated to compare the regression coefficients between the groups for each of the paths. With regards to the association between nonproductive thoughts and somatic symptoms, the regression coefficients significantly differed across the four groups (boys aged 11-14: $\beta = 0.61$ [0.51-0.70]; girls aged 11-14: $\beta = 0.52$ [0.42-0.62]; boys aged 15-20: $\beta = 0.39$ [0.31-0.48]; girls aged 15-20: $\beta = 0.46$ [0.37-0.55]). There was a significant difference between boys aged 11-14 and boys aged 15-20 (since the confidence intervals did not overlap across these groups). The non-significant result of the Wald test did not imply significant differences between the four groups in relation to the association between nonproductive thoughts and well-being factors.

2.3.2. Discussion

The main results of the present study showed that in a healthy representative adolescent sample higher rates of nonproductive thoughts predicted a higher level of somatic symptoms, while nonproductive thoughts presented negative relationships with each of the well-being factors. These results are completely in line with the existing empirical evidence, supporting the perseverative cognition hypothesis (Brosschot et al., 2006), namely that the different forms of recurrent negative thinking (e.g., rumination and worry) tend to prolong and maintain the stress-related psychophysiological arousal and may lead to a generalized pathogenic state, which may manifest in somatic symptoms or disorders (Ottaviani et al., 2016). This negative relationship is well-established and supported by previous findings in adolescents and children as well (Kökönyei et al., 2015; Lohaus et al., 2013).

Our findings on the relationship between rumination/worry and emotional, psychological and social well-being are also supported by other studies (Ciarrochi & Scott, 2006; Smith, Reynolds, Orchard, Whalley, & Chan, 2018). For instance, Harrington and Loffredo (2011) found that rumination was a significant negative predictor for three dimensions of well-being, albeit among university students. Further studies should extend their focus to measure the role of perseverative cognitions on well-being in adolescent samples as well, considering that mental health is more than just the absence of psychopathology (Nagy & Oláh, 2012).

Our findings also revealed that *the strength of the associations* between rumination/worry and somatic symptoms was invariant across genders but that it indicated significant differences between younger and older boys. In other words, the strength of the associations between rumination/worry and somatic symptoms showed gender invariance but the strength of the relationship significantly decreased with age among boys, while it remained unchanged among younger and older girls.

Our results are somewhat consistent with but also add to previous findings (Ottaviani, Shapiro, Davydov, Goldstein, & Mills, 2009) which indicate that there is an important shift

among boys around the age of 15 when vulnerability to rumination related somatic symptoms decreases. One could argue that for older boys, rumination or worry are more strongly associated with externalizing than with internalizing symptoms (Nolen-Hoeksema & Rusting, 1999). In a longitudinal study for example, rumination predicted subsequent aggressive behaviour among adolescent boys but not among girls (McLaughlin et al., 2014).

2.4 III. research question (Study III/3): Relationship between trait rumination and reward/punishment anticipation and consumption[3]

2.4.1. Methods

In our exploratory study, we analysed the associations of trait rumination and neural responses yielded for secondary (monetary) reward and punishment (loss) anticipation and consumption. Healthy volunteers aged between 18-38 years were recruited via newspaper and university advertisements. All volunteers were tested for eligibility by senior neurologist, psychiatrist and psychologist researchers.

Inclusion criteria were right-handedness assessed with a standardized handedness questionnaire (Oldfield, 1971), and normal or corrected to normal vision.

Exclusion criteria were any history of medical, neurological or psychiatric disorders, psychotropic drugs, substance use or any MRI contraindications (eg. metal implants).

Participants who met the inclusion criteria were asked to complete self-reported questionnaires including the above mentioned RRS (22-item version) and a depression scale (ZSDS; Zung Self-rating Depression Scale Zung, 1965; Simon, 1998).

After medical and psychological screening, participants underwent an fMRI scan session while they performed a variant of the classic monetary incentive delay task (MID) Knutson et al., 2001; Knutson et al., 2008), which was designed to evoke neural responses to monetary rewards and losses. The task has characterised extensively the neural bases of *anticipatory and consummator* stages of reward and loss processing (Dillon et al., 2008; Pizzagalli et al., 2009).

To capture the brain activation of anticipation, three contrasts were used: win cue-neutral cue [+ Ft versus 0 Ft] contrast, loss cue-neutral cue [- Ft versus 0 Ft] contrast and win cue-loss cue [+ Ft versus - Ft] contrast. The outcome phase of the task was also modelled by three contrasts: win outcome-neutral outcome, [You won versus No change], loss outcome-neutral outcome [You lost versus No change], and win outcome-loss outcome [You won versus You lost].

Altogether 37 healthy adults were involved in the study (15 men, mean age=25.92; SD=4.18 years)

2.4.2. Main results

To determine the influence of rumination on the brain activations related to monetary rewards and losses individual rumination scores were entered in the analyses as covariates. The analyses were controlled for age, sex, and ZSDS depression scores. Figure 2 shows the significant activated cluster.

[3] The present chapter is the copy of the following paper: Kocsel, N., Szabó, E., Galambos, A., Édes, A., Pap, D., Elliott, R., Kozák, L. R., Bagdy, Gy., Juhász, G. & Kökönyei, Gy. (2017). Trait rumination influences neural correlates of the anticipation but not the consumption phase of reward processing. *Frontiers in Behavioral Neuroscience, 11*:85.

The reward versus loss anticipation contrast [win cue-loss cue] showed significant positively correlated activations with RRS in one cluster, where the peaks were at the left inferior frontal gyrus pars triangularis, the left rolandic operculum and left anterior insula (see Table 3). No other contrast revealed significant brain activations in relation with RRS rumination scores, after FWE corrections.

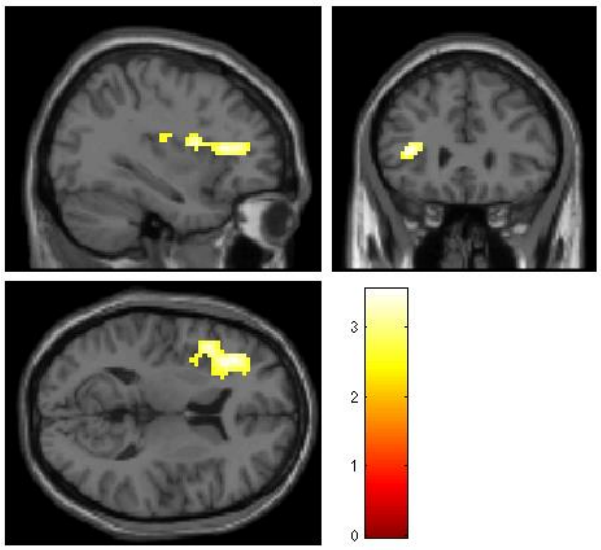

Figure 2. – Significant positive activations for win-loss anticipation contrast in correlation with rumination scores controlling for age, sex and ZSDS depression scores

Table 3- Activated regions in relation to trait rumination during win-loss anticipation

Contrast	Cluster size (voxel)	Region	Hemisphere	Peak T-value	Coordinates (MNI)		
					x	y	z
+ Ft vs. -Ft	311	Inferior frontal gyrus	Bal	3.55	-36	32	11
		Rolandic operculum	Bal	3.34	-42	-19	20
		anterior insula	Bal	3.33	-33	5	14

cluster level $p_{FWE}<0.05$

2.4.3. Discussion

In our study, we explored the neural correlates of trait rumination during reward and loss anticipation and consumption in a healthy, never depressed sample. Trait rumination was associated with reward anticipation (+ Ft vs. – Ft) showing significant activations in the regions of left anterior insula, left inferior frontal gyrus pars triangularis (IFG) and left rolandic

operculum. We did not detect any significant rumination-related activations yielded for reward or loss consumption (win-loss outcome).

Our results might indicate elevated sensitivity to reward cues among ruminators, since during reward anticipation they tended to more actively recruit brain areas together, such as anterior insula (AI) and inferior frontal gyrus (IFG), which are implicated in the *salience network* (SN) (Chang, Yarkoni, Khaw, & Sanfey, 2013; Menon, 2015; Wiech et al., 2010).

Our findings seem to concord with previous studies (Strigo, Simmons, Matthews, Craig, & Paulus, 2008; Wiech et al., 2010), where the authors found increased activation in AI during the anticipation but not the experience of pain stimuli. To date, increased SN activity associated with rumination was detected only for negatively-valenced stimuli (e.g. for monetary loss, pain), however, it is important to note that the participants in those studies were depressed or remitted depressed patients. For this reason, it is not clear whether these findings are connected directly to rumination or could be attributed to current or past depressed mood.

Besides the AI, we found rumination related peak activation in the left inferior frontal gyrus (IFG) pars triangularis during reward anticipation. The pars triangularis of the IFG, or more broadly the ventrolateral prefrontal cortex (vlPFC) (Ridderinkhof et al., 2004) has a central role in the prediction of reward information, abstract categorization and in the formation of stimulus - reward associations (Dixon & Christoff, 2014; Tanaka, Pan, Oguchi, Taylor, & Sakagami, 2015).

In addition, we detected heightened neural response during reward anticipation in the rolandic operculum (RO). Although, the exact role of RO in rumination is unclear, evidence suggests that increased RO activation is correlated with some anticipatory processes. For instance, obese adolescents showed greater activations in RO during anticipation of food reward than thin counterparts (Stice et al., 2008).

Our results suggest that for never depressed ruminators, potentially rewarding cues may be more salient than loss cues. These findings are in line with the work of Watkins and colleagues (2015), highlighting that rumination could be associated with abstract information processing mode and might lead to impaired anticipation of the future events. Our findings also shed light on the role of trait rumination in reward anticipation and might suggest that rumination alters processing of the motivational (wanting) aspect but not the hedonic (liking) aspect of monetary reward processing, at least in the absence of pathological mood.

2.5. <u>IV. research question (IV/4 study):</u> The association between trait perseverative cognitions, state rumination and resting HRV[4]

2.5.1. Methods

We hypothesized that trait rumination, trait worry (Visted et al., 2017; Williams et al., 2015, 2017), and spontaneously occurring intrusive thoughts during resting (state rumination) (Kühn et al., 2013, 2014) would show significant negative associations with resting HRV, even after controlling for the effects of recently experienced negative or positive, emotionally salient events (i.e. in the past 24 hours).

Resting HRV was recorded as beat-to-beat intervals (more precisely based on the distance of consecutive RR intervals=RMSSD) using the chest belts of FirstBeat TeamBelt. State

[4] The present chapter is the copy of the following paper: Kocsel, N., Köteles, F., Szemenyei, E., Szabó, E., Galambos, A. & Kökönyei, Gy. (2019). The association between perseverative cognition and resting heart rate variability: A focus on state ruminative thoughts. *Biological Psychology, 145*, 124-133.

rumination - conceptualized as repeatedly occurring, intrusive, negative or unwanted cognitions - were measured immediately after HRV recording by three items originally adapted from the Stress Coping Inventory (Brose et al., 2011). Trait perseverative cognitions were assessed by the ultra-brief version of Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990, Pajkossy et al., 2014) and The Ruminative Thought Style Questionnaire ((RTSQ; Brinker & Dozois, 2009).

Altogether 137 university students participated in the study, although we excluded 7 participants from further analysis. The final sample comprised 130 healthy young adults (118 females; mean age=23.86; SD=3.59 years).

2.5.2. Main results and discussion

To test the association between trait perseverative cognitions, state ruminative thoughts and lnRMSSD, a linear regression analysis was carried out. Results showed that lnRMSSD was independent of the scores of RTSQ and PSWQ, however, the increased level of state ruminative thoughts (even after controlling for recent life events) was significantly associated with lower lnRMSSD explaining 4.5 % of the variance (β=-0.219; t=-2.12; p=0.030).

Our important and novel finding was that a higher level of self-reported ruminative (intrusive) thoughts during resting HRV registration was negatively associated with HRV indexed by lnRMSSD scores.

Although trait rumination has been conceptualized as a putative answer for depressed mood in previous HRV studies (Williams et al., 2015), we hypothesized that HRV would be associated with a more general repetitive thinking process as well, which is independent of thought content and the cognitive-affective context. However, we did not find any significant associations between trait rumination, trait worry and resting HRV.

For this reason, we hypothesized that the non-significant results would have derived from the different conceptualization of the construct and resting HRV would have related to depressive rumination. In order to test this assumption we conducted another (IV/5) study.

2.6. <u>IV. research question (Study IV/5):</u> The relationship between adaptive/maladaptive trait and state rumination and resting HRV

2.6.1. Methods

Our main goal in this study was to replicate and confirm the findings of Study IV/4. In addition, we aimed to explore the relationship and interactions between the adaptive (reflective pondering) and maladaptive (brooding) aspects of (depressive mood related) trait rumination, state rumination and resting HRV (Schoofs et al., 2010; Treynor et al., 2003).

Altogether 90 participants were recruited, although we had to exclude 18 participants from the analyses. The final sample comprised 72 participants (58 females; mean age=22.24; SD=1.79 years). Trait rumination was measured by 10-item RRS (Treynor et al.,2003). State rumination, trait worry and resting HRV were measured by same instruments as in Study IV/4.

2.6.2. Main results and discussion

Although we found that mood-dependent trait rumination and trait worry were not significant predictors of resting HRV, we were able to confirm the results of Study IV/4, i.e. that state ruminative thoughts significantly explained individual differences in lnRMSSD (β=

-0.338; t=-2.72; p=0.008). In addition, the interaction between reflective pondering and state rumination turned out to be a significant independent variable of lnRMSSD (β=0.337; t=3.04; p=0.004).

In order to analyze these associations a further graphical moderation analysis was performed (ModGraph-I by Jose, 2013). Figure 3 demonstrates that when the level of trait reflection was high, the state ruminative thoughts did not have any effect on (relatively high) lnRMSSD scores. However, when the level of trait reflection was medium or low, state ruminative thoughts caused a decrease in lnRMSSD scores.

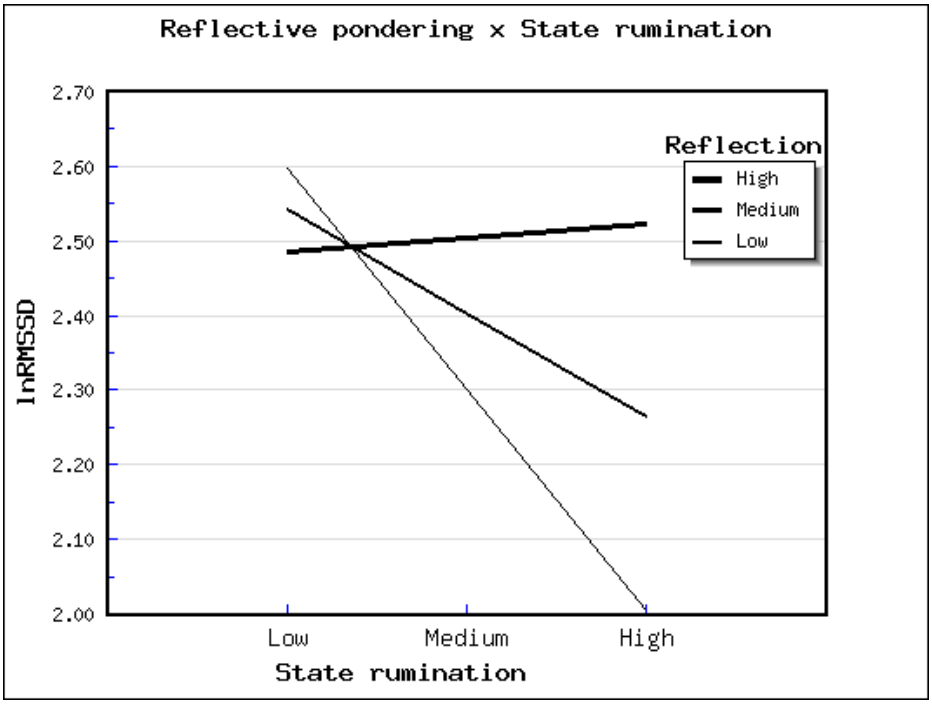

Figure 3.- Moderator role of reflective pondering in the relation of state ruminative thoughts and lnRMSSD

In this study we replicated the major finding of Study IV/4, namely that state ruminative thoughts were negatively associated with lnRMSSD during resting among healthy young adults. Given the dearth of empirical evidence, the interpretation of these findings may remain incomplete, although it does appear to confirm the results of neuroimaging resting state studies (Kühn et al., 2013, 2014), thereby indicating the importance of spontaneous state ruminative thoughts in brain-heart connections.

In contrast to previous results and our own expectations, we were not able to detect significant associations between trait rumination (brooding or reflection), trait worry and lnRMSSD during resting. In order to bridge the well-known conceptual and measurement gaps in the literature (Nolen-Hoeksema et al., 2008; Smith & Alloy, 2009), we used different instruments, such as RTSQ and RRS, across studies to assess trait rumination. However, in our analyses, trait rumination and trait worry were independent of lnRMSSD values.

Our findings seem to align with a meta-analysis (Ottaviani et al., 2016) which found that – at least in a healthy sample – only state perseverative cognitions were negatively correlated with HRV. Ottaviani and colleagues (2016) argue that rather than having physiological

consequences themselves, trait perseverative cognitions need to be triggered by an actual threat or stressor to elicit heart rate variability changes. This putative interplay between state and trait measures was also found in our study, i.e. trait reflection significantly moderated the relationship between state ruminative thoughts and lnRMSSD. This result suggests that trait reflective pondering is indeed a protective factor, especially against the effect of state rumination on lnRMSSD.

3. Summary of findings

Our first and second study indicated that trait rumination and trait worry significantly associated with the occurrence of subjective health complaints and led to reduced mental well-being among healthy adolescents as well. The reliable instruments we used lend further support to our findings, since we validated the Nonproductive Thoughts Questionnaires for Children. We also confirmed that the strength of the associations were invariant across genders, indicating that ruminative and worrying thoughts are equally associated with somatic symptoms and lower well-being among boys and girls (although age was a significant moderator).

In our third study, we confirmed that beyond the neural processing of negative emotional stimuli, trait rumination could influence neural responses during the anticipation of positive, potentially rewarding cues as well. To the best of our knowledge, this is the first study to show that trait rumination mainly relates to neural processing of motivational aspects of reward rather than hedonic aspect, at least in the absence of depressed mood.

In our fourth and fifth study, we pointed out that heart rate variability (HRV), considered as the physiological index of inflexible adaptation, associated with rumination, but instead of relating to general or dispositional ruminative response style, it associated with actual state rumination. However, trait reflective pondering had an important moderator role in protecting against state ruminative or intrusive thoughts.

4. Future directions

Our results indicate that beyond the context of mood or anxiety disorders it is worthwhile to investigate rumination among healthy people as well. Perseverative cognitions could influence mental and somatic health at subclinical level, and may have an impact on anticipatory processes and cardiovascular activity. Future studies are needed to clarify the relationship between reward processing and positive emotional stimuli and to explore the associations of trait rumination and HRV during anticipation. In addition, it would be beneficial to mix questionnaires and induction studies to see the correlations of state/trait rumination and HRV. Finally, it would be useful to apply an ecological valid framework to reveal whether our results hold any relationship with real life functioning or may carry any prognostic value on predicting changes in mental or somatic health.

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[5] The co-authors granted permission to use these publications in the dissertation

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