# Final Report for Grant 72/18, August 2021

Humans possess remarkable skills in predicting and understanding the mental states of others. However, significant interindividual variability in these skills exists, with poor socio-cognitive skills linked to problematic social behaviour. In particular, anxious-reactive temperament has been linked to slower development of mental state understanding in children. This project aims to improve our understanding of how different traits related to emotional reactivity are linked to social cognition under stress. Social situations are an important source of everyday stress. We propose that stressful situations reduce social cognition specifically in individuals high in emotional reactivity. This is explored in three studies investigating 1) the relationship between physiological regulation and social perspective taking under stress 2) the impact of stress on neural correlates of social cognition 3) the relationship between physiological regulation and self-predicted anger in social provocation scenarios.

## Theoretical background

The acquisition of socio-cognitive skills is a crucial aspect of development across childhood and adolescence. In children, social difficulties such as dysregulated aggression are among the most common behavioural problems for which parents seek professional help (Berkowitz, 1993; Blair, 2016). Later in life, deficits in social behaviour are linked to a number of psychiatric disorders (Association, 2013). Dysregulated aggression in childhood, a manifestation of maladaptive responding to social stimuli (DeWall et al., 2011), is strongly linked to internalizing anxiety problems (Bartels et al., 2018),(Granic, 2014). This suggests a link between high-reactive, anxious-avoidant temperament and poor socio-cognitive development. In a study using functional magnetic resonance imaging, we found that women with strong fear potentiation of the startle response – a physiological marker of fear reactivity

- showed reduced activity in the mentalizing network during an aggressive interaction (Beyer et al., 2014). Similarly, when avoiding aggressive interactions, increased amygdala activity – presumably reflecting a fear response - was accompanied by suppressed mentalizing activity (Buades-Rotger et al., 2017). Thus, our findings suggest, that high physiological reactivity to stress can acutely inhibit socio-cognitive processes.

In support of an influence of the physiological stress response on social cognition, studies found that children with low emotional reactivity showed higher ToM skills (Mink et al., 2014; Wellman et al., 2011). While research on the link between physiological regulation and socio-cognitive development in children is limited, there is support for such a relationship from animal studies. In rodents, aggressive animals tend to show reduced flexibility in response to environmental changes (Benus et al., 1990), higher endocrinological and sympathetic responses to stressors (Koolhaas et al., 2010; Sgoifo et al., 2014), and high impulsivity (Coppens et al., n.d.). A recent study in rats found, that selectively breeding for high stress reactivity resulted in increased aggression and anxiety (Walker et al., 2017). Together, these findings lend support to the idea that high physiological stress reactivity and poor physiological regulation are linked to deficits in social functioning.

Typically investigated measures of physiological stress reactivity and stress regulation are heart rate as a measure of arousal, and heart rate variability (HRV) as a measure of vagal / parasympathetic control over heart rate. HRV is seen as a measure of prefrontal cortical function (Thayer et al., 2009) and is positively related to emotion recognition and regulation (Quintana et al., 2012; Ruiz-Padial et al., 2003; Visted et al., 2017; Yang & Friedman, 2017), and negatively to the attribution of blame in an anger-evoking scenario (León et al., 2009). In line with a link between physiological regulation and socio-cognitive functioning, a study in kindergarteners showed stronger HRV reductions and heart rate increases in response to emotional film clips in children with poorer pro-social functioning (Kalvin et al., 2016).

In rodent models of stress reactivity, regular exercise leads to an overall decrease in resting heart rate, and has a moderate effect on HRV (Carnevali & Sgoifo, 2014). Arrhythmia-protective effects of voluntary exercise persist after the termination of training, suggesting a long-term protective effect of exercise on cardiovascular functioning (Beig et al., n.d.; Carnevali & Sgoifo, 2014). Similarly, voluntary exercise in hamsters has a protective effect against anxiety and submission behaviour following a stressful experience of social defeat (Kingston et al., 2018).

Many studies on human participants have shown anxiolytic effects of exercise (Wipfli et al., 2008). Moreover, beneficial effects of physical fitness on regulation of cardiovascular reactivity to stress are well-established (Huang et al., 2013). Exercise programs of 12 weeks or more have been shown to increase HRV and decrease physiological stress reactivity (Klaperski et al., 2014; Von Haaren et al., 2016). In elite athletes, reduced reactivity to psychosocial stress has been observed (Rimmele et al., 2007). Converging evidence of blunted stress reactivity after physical exercise suggests, that regular exercise may reduce the impact of stressful life events (Hamer et al., 2006; Roemmich et al., 2009).

This project investigates the relationship between HRV as a measure of cardiovascular regulation, physical activity as a well-known regulator of acute stress responses, and behavioural and neural measures of socio-cognitive functioning under stress.

**Study 1: The relationship between heart-rate variability, physical activity and spontaneous social perspective taking under stress**

76 healthy female adult volunteers participated in this study, with the data of 59 included in the final analysis. All procedures were approved by the Queen Mary University research ethics committee.

Materials

The main task used in this study was a target detection task designed to measure spontaneous social perspective taking (El Kaddouri et al., 2019; Kovács et al., 2010). This task is set up as a reaction time task, in which participants respond to stimuli presented on a computer screen. In each trial of this task, participants observe a short animated video of an agent placing a ball on a table. In the middle of the table, there is an occluder. The ball rolls behind the occluder and either remains there or rolls out of the frame on the other side of the screen, before the agent leaves the scene. The ball then reappears and, in the agent's absence, either stops behind the occluder or outside the frame. Thus, four experimental conditions are formed, based on the agent's and the participant's belief regarding the location of the ball: A+P+ (both believe the ball to be behind the occluder), A-P- (both believe the ball not to be behind the occluder), A-P+ (the agent believes the ball not to be behind the occluder, the participant believes it to be present) and A+P- (the agent believes the ball to be present behind the occluder, the participant beliefs it to be absent). The agent then returns and the occluder drops. If the ball is behind the occluder, participants are asked to instructed to respond by button press as quickly as possible. The presence of the ball is random at 50%, independent of belief conditions. Trials in which the ball is absent are not analysed, as there are no valid reaction times. Generally, participants are faster at responding to the ball's presence when they believed it to be present. The trials of interest are the A+P- and A-P- conditions, in which the participant believes the ball to be absent. For these, on average participants tend to be faster if the agent believed the ball to be present, reflecting spontaneous representation of the agent's mental state. The difference in reaction times A-P- MINUS A+P- is called the Theory-of-Mind index (ToM-index).

As a stress induction, we used the well-established mental arithmetic stress task, in which participants are instructed by the experimenter to perform difficult progressive subtraction under time pressure (Jern et al., 1991). As a control condition, we used non-stressful word search tasks.

As measures of physiological regulation, we measured participant's resting heart-rate variability (HRV), as well as self-reported exercise levels in hours / week on average.

Procedures

Participants were informed about the study methods and provided informed consent. Resting heart rate measures were then collected.

Participants then underwent one of two blocks of the ball detection task. One block was combined with 2 minutes of stress induction prior to each 5 minutes of the task, the other was combined with the non-stressful control task. Block order was counterbalanced between participants.

Data analysis

We split participants into two groups based on their exercise levels: low (less than one hour exercise per week; n = 28) and high (more than one hour exercise per week, n = 31). We then set up linear regression models to assess whether HRV and exercise frequency predicted ToM-index in the control condition and ToM-index in the stress condition.

Results

For $ToM_{control}$, the regression was significant ($R^2$=.1, p =.05), with HRV the only significant predictor (β=-.288, p=.031). For $ToM_{stress}$, the regression was also significant ($R^2$=.13, p =.02), with exercise as significant predictor (β=.36, p=.006). Post-hoc comparisons showed that under stress, participants in the high exercise group showed a higher ToM-index than participants in the low exercise group.

Online replication study

To assess the impact of lifelong exercise, the same study setup was used in an online experimental study, using a computerised version of the stress induction. HRV was not assessed, and lifelong exercise was measured.

Data from 96 participants was collected (F = 31, M = 65), with 87 included in the analysis.

The only significant effect was childhood exercise predicting $ToM_{control}$ (β= 4.53, p = .014). However, both $ToM_{control}$ (M = 5.28, SD = 83.59) and $ToM_{stress}$ (M = 15.24, SD = 65.17) showed great variability, indicating unreliable measures of reaction time or issues with attention in the online setting.

**Study 2: the impact of stress on neural correlates of social cognition**

Data from 54 participants is included in the analysis, exceeding the originally planned sample of n = 40, due to the need for greater statistical power to include the between subject factor of exercise, and the availability of additional research funds through QMUL for increasing the sample size.

Materials

The same ball detection task as in study 1 was used, in combination with a computerized version of the stress induction and a non-stressful anagram task. To prevent order effects from affecting interindividual variability, an ABBA design was used with all participants first performing one control block, then two stress blocks, and one more control block.

This task was conducted in combination with functional magnetic resonance imaging (fMRI) to measure BOLD signal as an indicator of neural activity.

Heart rate variability was measured following the MRI measurement.

Current exercise levels were measured ahead of the scanning session in an online questionnaire, to ensure equal distribution of participants with high and low exercise levels.

Data analysis

MRI data were analysed using SPM12. The main contrast of interest at the single subject level was INC>CON: INC describes trials in which the agent's and participant's believes are incongruent (A+P-, A-P+), CON those where they are congruent (A+P+, A-P-). Due to habituation effects across task runs, we also analysed each of the four runs separately.

We performed a region of interest (ROI) analysis focusing on the right temporo-parietal junction (rTPJ), defined as a 5mm sphere around the coordinates [57, -52, 34].

Results

The INC > CON contrast showed increased activity in the rTPJ for the first run ($t = 7.99$, $p < .001$), which belonged to the control condition, and the second run ($t = 2.52$, $p = .015$), which belonged to the stress condition. Run 3 and 4 showed no significant activity ($p > .2$). We therefore concentrated the following analyses on those two runs.

Contrary to our hypothesis, activity in the rTPJ was higher in the stress condition (run 2), than in the control condition (run 1; $t = 2.38$, $p = .021$).

Exercise was significantly and positively correlated with rTPJ activity in the control run ($r = .288$, $p = .035$), but not the stress run ($r = -.233$, $p = .091$). HRV was negatively correlated with rTPJ activity in the stress run ($r = -.281$, $p = .038$), but not the control run ($r = .114$, $p = .406$).

**Study 3**

This study uses the same dataset as study 1, thus data from the same participants is analysed.

Materials

The same exercise measure as reported for study 1 was used.

To assess predicted anger, participants were given four hypothetical scenarios designed to induce frustration and anger. Two were non-social (being delayed on the bus; a website crashing after spending a long time entering information), one involved an unambiguous provocation from a stranger (someone cutting in line), and one an ambiguous provocation from a friend (being stood up at a restaurant). Participants were then asked to rate for various emotions including anger, how strongly they would experience that emotion in the given situation.

Data analysis

We set up a multilevel linear model analysis to assess the impact of scenario type, HRV, and exercise group on anger ratings.

Results

We found a main effect of one scenario ($\beta$=26.0, $p$ =.007), with the social-unambiguous scenario eliciting higher anger than the social-ambiguous scenario. We also found a main effect of exercise ($\beta$=-22.510, $p$ = .001) with participants in the high exercise group reporting lower anger than participants in the low exercise group, and an interaction between exercise and HRV ($\beta$=.5, $p$ = .023). Post-hoc analysis showed that in the high exercise group only, there was a positive relationship between HRV and anger ($\beta$=.77, $p$ = .003).

## Discussion

This project examined the link between physiological regulation and social cognition under stress. We found a strong link between self-reported physical exercise, and spontaneous perspective taking under stress. High-exercise participants also predicted lower anger in frustrating situations. Across participants, acute stress reduced reactivity of brain areas associated with social cognition.

Our findings from studies 1 and 3 suggest that physical exercise, as a known moderator of stress reactivity, plays an important role in social functioning. Participants who reported not to engage in regular exercise showed lower social cognition under stress than participants in the high-exercise group. The latter also scored lower on anger ratings for frustrating scenarios. This is in line with the assumption that particularly in negatively arousing situations, engaging in social cognition supports the consideration of alternative viewpoints, allowing for more benign interpretations and therefor resulting in lower anger.

Our MRI study showed a positive correlation between exercise levels and activity in a key mentalizing region, the rTPJ, in the first run of our task, but not later runs. Overall, our findings point towards habituation across task runs, with no mentalizing activity observed for runs 3 and 4. Nevertheless, given that MRI environments in themselves can be stressful, especially early during the scanning session, these findings are tentatively in line with the results from study 1.

For HRV, a negative correlation was observed with rTPJ activity under stress, an unexpected finding. One possible explanation of this finding is that participants with higher HRV (an index of physiological regulation) showed faster habituation towards the paradigm, and thus reduced mentalizing activity in run 2 (irrespective of the stress induction).

Overall, our findings point towards the importance of overall arousal levels. In the online study, participants were completing the tasks from home, thus presumably in a low-stress, familiar environment. In this context, the stress induction did not appear to significantly affect task performance- indeed, ToM-index was descriptively higher in the stress condition, suggesting that the induction moved participants towards more optimal arousal levels. The

MRI environment, in contrast, is a mildly stressful situation in itself, and any additional stress induction might either not affect arousal levels, or move participants towards sub-optimally high levels of arousal.

**Publication of data**

Findings from study 1 and 3 are published in the peer reviewed journal *Stress*:

Kähkönen, J. E., Krämer, U. M., Buades-Rotger, M., & Beyer, F. (2021). Regulating interpersonal stress: the link between heart-rate variability, physical exercise and social perspective taking under stress. *Stress*, 1-10.

Findings from study 2 will be submitted for publication once data analysis and writeup are complete (foreseeably late 2021).

## References


Association, A. P. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub.

Bartels, M., Hendriks, A., Mauri, M., Krapohl, E., Whipp, A., Bolhuis, K., Conde, L. C., Luningham, J., Ip, H. F., & Hagenbeek, F. (2018). Childhood aggression and the co-occurrence of behavioural and emotional problems: Results across ages 3–16 years from multiple raters in six cohorts in the EU-ACTION project. *European Child & Adolescent Psychiatry*, *27*(9), 1105–1121.

Beig, M. I., Callister, R., Saint, D. A., Bondarenko, E., Walker, F. R., Day, T. A., & Nalivaiko, E. (n.d.). Voluntary exercise does not affect stress-induced tachycardia, but improves resistance to cardiac arrhythmias in rats. *Clinical and Experimental Pharmacology and Physiology*, *38*(1), 19–26. https://doi.org/10.1111/j.1440-1681.2010.05456.x

Benus, R. F., Daas, S. D., Koolhaas, J. M., & Oortmerssen, G. a. V. (1990). Routine Formation and Flexibility in Social and Non-Social Behaviour of Aggressive and Non-Aggressive Male Mice. *Behaviour*, *112*(3), 176–193. https://doi.org/10.1163/156853990X00185

Berkowitz, L. (1993). *Aggression: Its causes, consequences, and control.* Mcgraw-Hill Book Company.

Beyer, F., Münte, T. F., Erdmann, C., & Krämer, U. M. (2014). Emotional reactivity to threat modulates activity in mentalizing network during aggression. *Social Cognitive and Affective Neuroscience*, *9*(10), 1552–1560. https://doi.org/10.1093/scan/nst146

Blair, R. J. (2016). The neurobiology of impulsive aggression. *Journal of Child and Adolescent Psychopharmacology*, *26*(1), 4–9.

Buades-Rotger, M., Beyer, F., & Krämer, U. M. (2017). Avoidant Responses to Interpersonal Provocation Are Associated with Increased Amygdala and Decreased Mentalizing Network Activity. *ENeuro*, ENEURO.0337-16.2017. https://doi.org/10.1523/ENEURO.0337-16.2017

Carnevali, L., & Sgoifo, A. (2014). Vagal modulation of resting heart rate in rats: The role of stress, psychosocial factors, and physical exercise. *Frontiers in Physiology*, *5*, 118. https://doi.org/10.3389/fphys.2014.00118

Coppens, C. M., Boer, S. F. de, Buwalda, B., & Koolhaas, J. M. (n.d.). Aggression and aspects of impulsivity in wild-type rats. *Aggressive Behavior*, *40*(4), 300–308. https://doi.org/10.1002/ab.21527

DeWall, C. N., Anderson, C. A., & Bushman, B. J. (2011). The general aggression model: Theoretical extensions to violence. *Psychology of Violence*, *1*(3), 245.

El Kaddouri, R., Bardi, L., De Bremaeker, D., Brass, M., & Wiersema, J. R. (2019). Measuring spontaneous mentalizing with a ball detection task: Putting the attention-check hypothesis by Phillips and colleagues (2015) to the test. *Psychological Research*. https://doi.org/10.1007/s00426-019-01181-7

Granic, I. (2014). The role of anxiety in the development, maintenance, and treatment of childhood aggression. *Development and Psychopathology*, *26*(4pt2), 1515–1530.

Hamer, M., Taylor, A., & Steptoe, A. (2006). The effect of acute aerobic exercise on stress related blood pressure responses: A systematic review and meta-analysis. *Biological Psychology*, *71*(2), 183–190. https://doi.org/10.1016/j.biopsycho.2005.04.004

Huang, C.-J., Webb, H. E., Zourdos, M. C., & Acevedo, E. O. (2013). Cardiovascular reactivity, stress, and physical activity. *Frontiers in Physiology*, *4*, 314. https://doi.org/10.3389/fphys.2013.00314

Jern, S., Pilhall, M., Jern, C., & Carlsson, S. G. (1991). Short-term reproducibility of a mental arithmetic stress test. *Clinical Science*, *81*(5), 593–601.

Kalvin, C. B., Bierman, K. L., & Gatzke-Kopp, L. M. (2016). Emotional Reactivity, Behavior Problems, and Social Adjustment at School Entry in a High-risk Sample. *Journal of Abnormal Child Psychology*, *44*(8), 1527–1541. https://doi.org/10.1007/s10802-016-0139-7

Kingston, R. C., Smith, M., Lacey, T., Edwards, M., Best, J. N., & Markham, C. M. (2018). Voluntary exercise increases resilience to social defeat stress in Syrian hamsters. *Physiology & Behavior*, *188*, 194–198. https://doi.org/10.1016/j.physbeh.2018.02.003

Klaperski, S., von Dawans, B., Heinrichs, M., & Fuchs, R. (2014). Effects of a 12-week endurance training program on the physiological response to psychosocial stress in men: A randomized controlled trial. *Journal of Behavioral Medicine*, *37*(6), 1118–1133. https://doi.org/10.1007/s10865-014-9562-9

Koolhaas, J. M., de Boer, S. F., Coppens, C. M., & Buwalda, B. (2010). Neuroendocrinology of coping styles: Towards understanding the biology of individual variation. *Frontiers in Neuroendocrinology*, *31*(3), 307–321. https://doi.org/10.1016/j.yfrne.2010.04.001

Kovács, Á. M., Téglás, E., & Endress, A. D. (2010). The social sense: Susceptibility to others' beliefs in human infants and adults. *Science (New York, N.Y.)*, *330*(6012), 1830–1834. https://doi.org/10.1126/science.1190792

León, I., Hernández, J. A., Rodríguez, S., & Vila, J. (2009). When head is tempered by heart: Heart rate variability modulates perception of other-blame reducing anger. *Motivation and Emotion*, *33*(1), 1–9. https://doi.org/10.1007/s11031-008-9112-2

Mink, D., Henning, A., & Aschersleben, G. (2014). Infant shy temperament predicts preschoolers Theory of Mind. *Infant Behavior & Development*, *37*(1), 66–75. https://doi.org/10.1016/j.infbeh.2013.12.001

Quintana, D. S., Guastella, A. J., Outhred, T., Hickie, I. B., & Kemp, A. H. (2012). Heart rate variability is associated with emotion recognition: Direct evidence for a relationship between the autonomic nervous system and social cognition. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *86*(2), 168–172. https://doi.org/10.1016/j.ijpsycho.2012.08.012

Rimmele, U., Zellweger, B. C., Marti, B., Seiler, R., Mohiyeddini, C., Ehlert, U., & Heinrichs, M. (2007). Trained men show lower cortisol, heart rate and psychological responses to psychosocial stress compared with untrained men. *Psychoneuroendocrinology*, *32*(6), 627–635. https://doi.org/10.1016/j.psyneuen.2007.04.005

Roemmich, J. N., Lambiase, M., Salvy, S. J., & Horvath, P. J. (2009). Protective effect of interval exercise on psychophysiological stress reactivity in children. *Psychophysiology*, *46*(4), 852–861. https://doi.org/10.1111/j.1469-8986.2009.00808.x

Ruiz-Padial, E., Sollers, J. J., Vila, J., & Thayer, J. F. (2003). The rhythm of the heart in the blink of an eye: Emotion-modulated startle magnitude covaries with heart rate variability. *Psychophysiology*, *40*(2), 306–313.

Salmon, P. (2001). Effects of physical exercise on anxiety, depression, and sensitivity to stress: A unifying theory. *Clinical Psychology Review*, *21*(1), 33–61. https://doi.org/10.1016/S0272-7358(99)00032-X

Sgoifo, A., Carnevali, L., & Grippo, A. J. (2014). The socially stressed heart. Insights from studies in rodents. *Neuroscience & Biobehavioral Reviews*, *39*, 51–60. https://doi.org/10.1016/j.neubiorev.2013.12.005

Sothmann, M. S., Buckworth, J., Claytor, R. P., Cox, R. H., White-Welkley, J. E., & Dishman, R. K. (1996). Exercise Training and the Cross-Stressor Adaptation Hypothesis. *Exercise and Sport Sciences Reviews*, *24*(1), 267.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: The neurovisceral integration perspective on self-regulation, adaptation, and health. *Annals of Behavioral Medicine: A Publication of the Society of Behavioral Medicine*, *37*(2), 141–153. https://doi.org/10.1007/s12160-009-9101-z

Visted, E., Sørensen, L., Osnes, B., Svendsen, J. L., Binder, P.-E., & Schanche, E. (2017). The Association between Self-Reported Difficulties in Emotion Regulation and Heart Rate Variability: The Salient Role of Not Accepting Negative Emotions. *Frontiers in Psychology*, *8*, 328. https://doi.org/10.3389/fpsyg.2017.00328

Von Haaren, B., Ottenbacher, J., Muenz, J., Neumann, R., Boes, K., & Ebner-Priemer, U. (2016). Does a 20-week aerobic exercise training programme increase our capabilities to buffer real-life stressors? A randomized, controlled trial using ambulatory assessment. *European Journal of Applied Physiology*, *116*(2), 383–394.

von Haaren, B., Ottenbacher, J., Muenz, J., Neumann, R., Boes, K., & Ebner-Priemer, U. (2016). Does a 20-week aerobic exercise training programme increase our capabilities to buffer real-life stressors? A randomized, controlled trial using ambulatory assessment. *European Journal of Applied Physiology*, *116*(2), 383–394. https://doi.org/10.1007/s00421-015-3284-8

Walker, S. E., Zanoletti, O., Guillot de Suduiraut, I., & Sandi, C. (2017). Constitutive differences in glucocorticoid responsiveness to stress are related to variation in aggression and anxiety-related behaviors. *Psychoneuroendocrinology*, *84*, 1–10. https://doi.org/10.1016/j.psyneuen.2017.06.011

Wellman, H. M., Lane, J. D., LaBounty, J., & Olson, S. L. (2011). Observant, nonaggressive temperament predicts theory of mind development. *Developmental Science*, *14*(2), 319–326. https://doi.org/10.1111/j.1467-7687.2010.00977.x

Wipfli, B. M., Rethorst, C. D., & Landers, D. M. (2008). The Anxiolytic Effects of Exercise: A Meta-Analysis of Randomized Trials and Dose–Response Analysis. *Journal of Sport and Exercise Psychology*, *30*(4), 392–410. https://doi.org/10.1123/jsep.30.4.392

Yang, X., & Friedman, B. H. (2017). Individual differences in behavioral activation and cardiac vagal control influence affective startle modification. *Physiology & Behavior*, *172*, 3–11. https://doi.org/10.1016/j.physbeh.2016.06.004