

VEDENJSKE POTEZE AGRESIVNOSTI PRI OSEBAH, IZPOSTAVLJENIH PRENATALNEMU STRESU

Urška Smrke, Lilijana Šprah

Znanstvenoraziskovalni center Slovenske akademije znanosti in umetnosti,
Družbenomedicinski inštitut

<http://dmi.zrc-sazu.si/sl#v>

Raziskavo sofinancira Javna agencija za raziskovalno dejavnost Republike Slovenije, št. projekta J3-6801.



PRENATALNI STRES

= stres, ki ga doživlja mama v času nosečnosti in lahko (negativno) učinkuje na razvoj otroka

▪povečano tveganje za kardiovaskularne bolezni, debelost, izkrivljen motorični razvoj, epilepsijo (1)

Increased anxiety

O'Connor, Heron, & Glover, 2002; Van Den Bergh & Marcoen, 2004; Bergman et al., 2007; de Bruijn et al., 2009

Increased ADHD

More readily distracted attention
Increased impulsivity

O'Connor, Heron, Golding et al., 2002; Obel, Henriksen et al., 2003; Huizink et al., 2002; Rodriguez & Bohlin, 2005; Van Den Bergh & Marcoen, 2004

Increased conduct disorder

Breaking rules
Increased aggression

O'Connor, Heron, & Glover, 2002; Van Den Bergh & Marcoen, 2004; de Bruijn et al., 2009; Rice et al., 2010; E. D. Barker & Maughan, 2009

Lower cognitive performance

Bergman et al., 2007; Laplante et al., 2008; Mennes et al., 2006; Huizink et al., 2003)

More mixed handedness

Obel, Hedegaard et al., 2003; Glover et al., 2004; Rodriguez & Waldenstrom, 2008

Altered function of the HPA axis

O'Connor et al., 2005; Yehuda et al., 2005; Gutteling et al., 2005; Huizink et al., 2008; Van den Bergh et al., 2008; Entringer, Kumsta et al., 2009

Fewer male offspring

Peterka et al., 2004; Obel et al., 2007

(1) Cottrell in Seckl, 2009

(2) Glover, 2011

PRENATALNI STRES

- negativni učinki prenatalnega stresa kot **rezultat podaljšane izpostavljenosti fetusa povišanim nivojem kortizola** (3)
 - povečano izločanje kortizola v nosečnosti se povezuje z *nižjo porodno težo, povišanim neonatalnim nivojem kortizola in z dolgotrajnimi učinki na psihološki razvoj* (4)
- **prenatalni stres → trajne spremembe v nevrottransmitterskem sistemu → možna povečana ranljivost za težave v duševnem zdravju**
 - *povezave z razpoloženskimi motnjami, shizofrenijo, zlorabo psihoaktivnih substanc, vedenjskimi motnjami, motnjami spanja* (5)

(3) npr. Huizink idr., 2003

(4) npr. Bergman idr., 2007; Khashan idr., 2008

(5) Field in Diego, 2008

PRENATALNI STRES IN AGRESIVNOST

- prenatalni stres potencialno lahko učinkuje na spremembe funkcije HPA osi
 - **spremenjena aktivnost HPA osi + nizki bazalni nivoji kortizola + zmanjšan odziv na stres → potencialni biološki markerji** nekaterih motenj poznanjenja, še posebej **agresivnosti** (6)
 - vendar: nujno še proučevanje interakcije genetskih, bioloških in socialnih faktorjev za bolj jasno razumevanje povezave med HPA osjo in psihopatologijo (7)
- antisocialno vedenje bolj verjetno pri otrocih mater izpostavljenih povečanemu stresu, anksioznosti ali depresiji v času nosečnosti (8)
 - npr. možno kot **adaptacija fetusa na pričakovane nezaželene oz. škodljive pogoje postnatalnega okolja** (9)

(6) Gowin idr., 2013; Platje idr., 2013; Popma idr., 2007; Poustka idr., 2010

(7) Alink idr., 2008; Buchmann idr., 2014

(8) Hay idr., 2010

(9) Bachmann idr., 2014

PRENATALNI STRES IN SPOL

Abstract An increased incidence of anxiety, depression and attention deficits in children has been linked to psychological stress during pregnancy. Subjection of a pregnant rat to stress at a time when the foetal limbic and hypothalamic pituitary adrenal (HPA) axes develop results in anxiogenic and depressive behaviour and learning and attention deficits in the offspring, which depend on its gender, intensity and timing of the maternal stress and behaviour being tested. Maternal stress increases corticosterone levels in the foetal brain, decreases foetal testosterone and brain aromatase activity in males, and alters brain catecholamine activity to that in females. Learning deficits, reductions in hippocampal neurogenesis, LTP and dendritic spine density in the prefrontal cortex are more readily seen in prenatally-stressed males, while anxiety, depression and increased response of the HPA axis to stress are more prevalent in females. Genders may differ in the sensitivity of developing brain areas to stress hormones.

(10)

A B S T R A C T

Background: Sex differences are found in animal studies concerning the relationship between prenatal maternal stress and outcome of the offspring. Most human studies in this field have not addressed sex differences, although differences between boys and girls may elucidate the biochemical as well as psychological processes involved. Associations between prenatal maternal emotional complaints and behavioural problems of toddlers and preschoolers as assessed by both mothers and fathers are studied separately for boys and girls.

Methods: Healthy Dutch Caucasian singleton, pregnant women ($N=444$) answered questionnaires about anxiety and depression in every trimester of pregnancy. When their children (227 boys, 217 girls) were between 14 and 54 months old, both parents reported on their current feelings of depression and anxiety and on the behavioural problems of their children.

Results: Prenatal maternal emotional complaints were found to be associated with child behavioural problems both in boys and in girls, but in different ways. Prenatal maternal emotional complaints during the first trimester were associated with total and internalizing behavioural problems for boys. Emotional complaints during the third trimester were associated with total, internalizing, as well as externalizing behavioural problems for girls.

Conclusions: Differentiation according to sex and information on timing of emotional complaints during pregnancy is needed in studies concerning the relation between prenatal maternal emotional complaints and child outcome.

(11)

(10) Weinstock, 2007

(11) de Bruijn idr., 2009

ŠTUDIJE PRENATALNEGA STRESA IN OPREDELITEV STRESNEGA DOGODKA

- možni stresni dogodki za preučevanje prenatalnega stresa: psihološka travma, izguba zaposlitve, smrt partnerja, huda poškodba, izkušnje naravnih katastrof,... (12)
 - nekatere je mogoče tudi bolj objektivno določiti v smislu intenzivnosti in trajanja (npr. potresi, teroristični napadi, vojne) (13)

27. 6. – 7. 7. 1991: 10-dnevna vojna za Slo.

(12) npr. Robinson idr., 2009; Dancause idr., 2011; Harville idr., 2010

(13) Gaignic-Philippe idr., 2014

NAMEN

- preliminarni pregled izraženosti vedenjskih potez agresivnosti pri potomcih mater, izpostavljenih 10-dnevni vojni
(v primerjavi s potomci mater, nosečih pred in po vojni)

PSIHOLOŠKE IN REPRODUKTIVNE MOTNJE PRI MOŠKIH, IZPOSTAVLJENIH PRENATALNEMU STRESU

- psihološka študija
- androloška študija (reproduktivno zdravje moških, izpostavljenih prenatalnemu stresu)
- študija živalskih modelov

METODA: UDELEŽENCI

3 skupine: prenatalno obdobje glede na 10-dnevno vojno

Skupina	Vsi	Moški	Ženske
	N (% celotnega N)	N (% skupine)	N (% skupine)
Pred vojno (kontrolna skupina 1) [1. 9. 1990 – 31. 3. 1991]	169 (21,8 %)	88 (52,1 %)	81 (47,9 %)
Med vojno (nosečnost) * [30. 6. 1991 – 8. 3. 1992]	284 (36.6 %)	172 (60,8 %)	111 (39,2 %)
Po vojni (kontrolna skupina 2) ** [1. 4. 1992 – 31. 12. 1992]	323 (41.6 %)	208 (65,0 %)	112 (34,7 %)
Skupaj	776 (100.0 %)	468 (60.3 %)	304 (39,2 %)

* Manjkajoč podatek o spolu za 1 udeleženca.

** Manjkajoč podatek o spolu za 3 udeležence.

METODA: INSTRUMENTI

Buss-Perryjev vprašalnik agresivnosti BPAQ (14)

- fizična agresivnost (9 postavk; $\alpha = 0,71$)
- besedna agresivnost (5 postavk; $\alpha = 0,56$)
- jeza (7 postavk; $\alpha = 0,74$)
- sovraštvo (8 postavk; $\alpha = 0,76$)

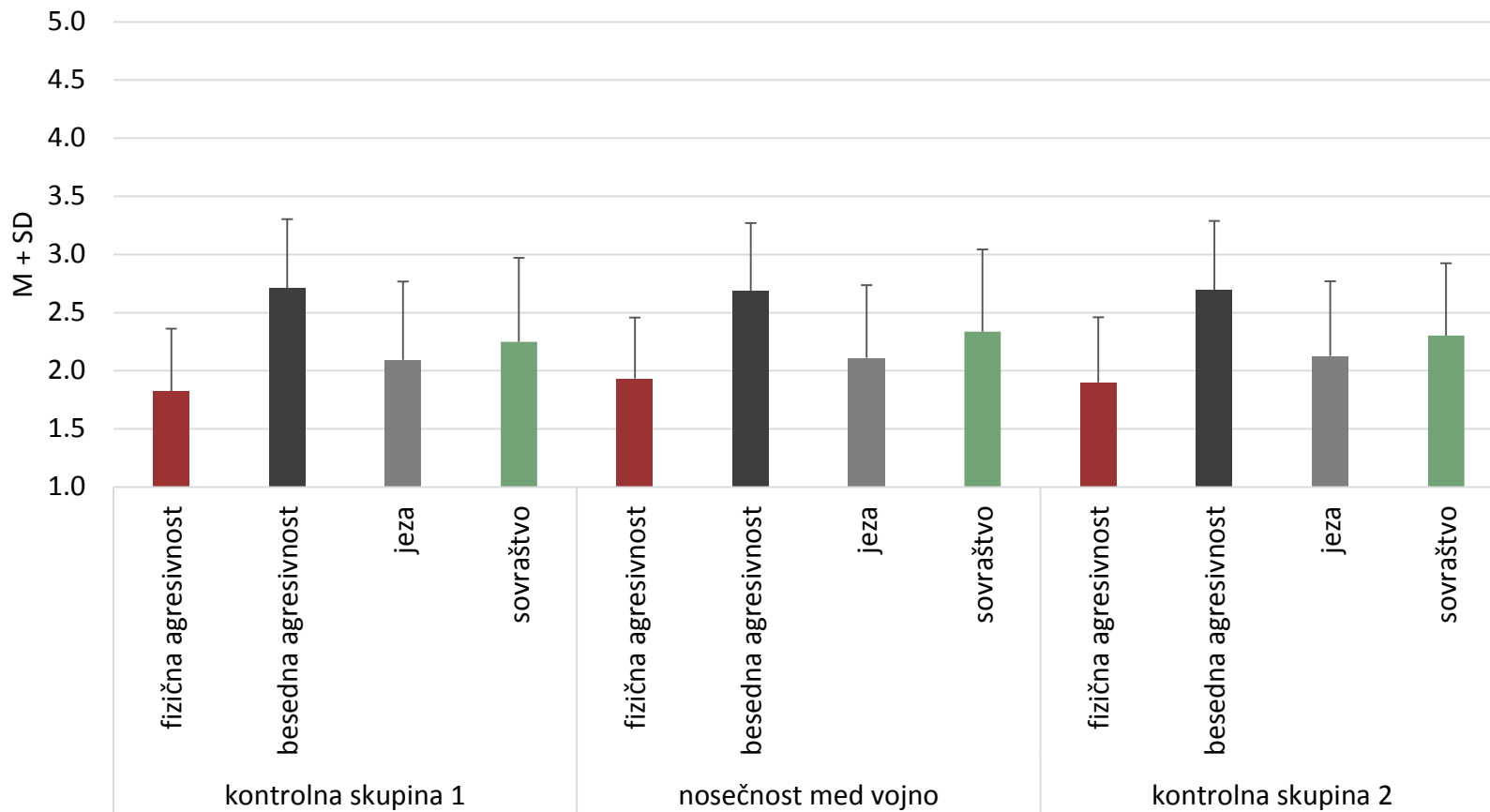
+ vprašalnik z demografskimi spremenljivkami

METODA: POSTOPEK IN STATISTIČNE ANALIZE

- udeleženci iz fakultet UL in UM (od oktobra 2014 do maja 2016)
- pogoj za sodelovanje: podpisano soglasje in datum rojstva od 1.9.1990 do 31.12.1992

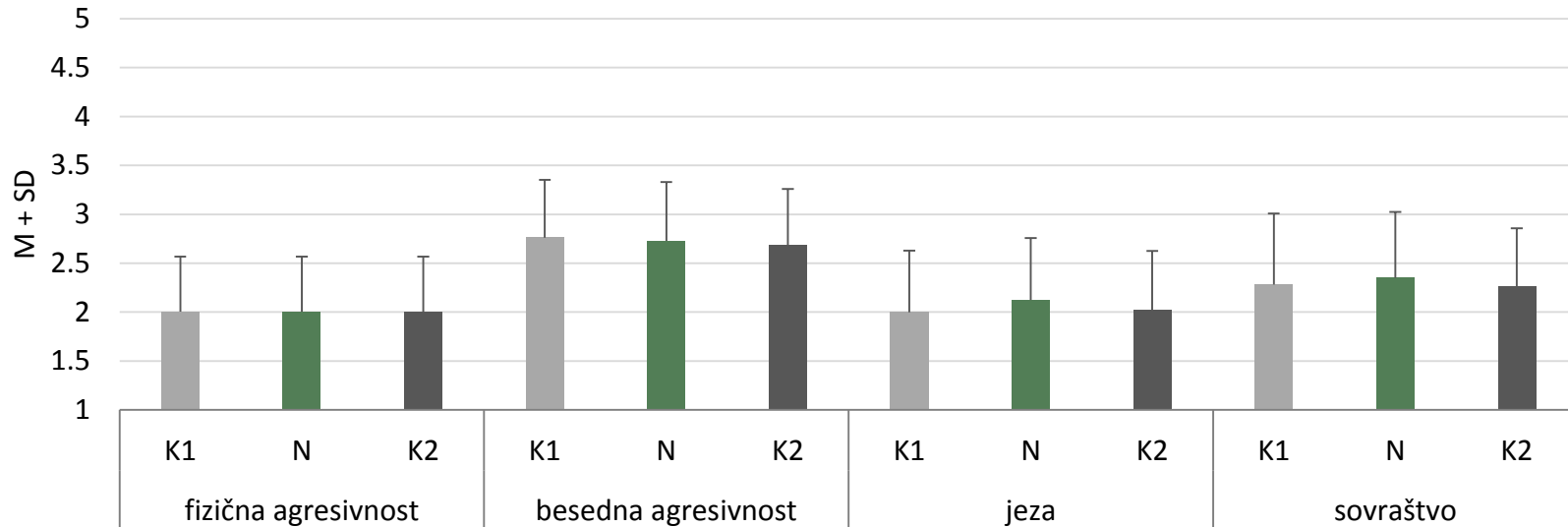
- ANOVA, zankanje

REZULTATI



Slika 1. Povprečni dosežki skupin na podlestvicah agresivnosti

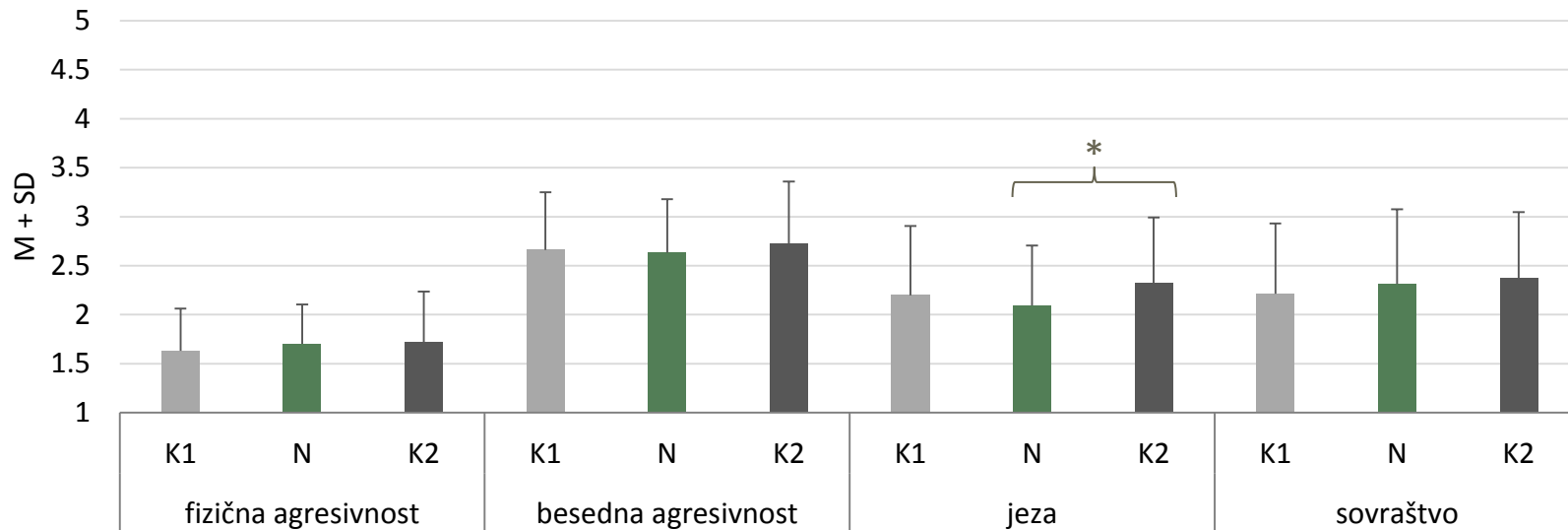
REZULTATI: MOŠKI



Slika 2. Povprečni dosežki skupin na podlestvicah agresivnosti (moški)

- fizična agresivnost: $F(1,465) = 1,292, p = 0,276, r = 0,074$
- besedna agresivnost: $F(1,465) = 0,547, p = 0,579, r = 0,048$
- jeza: $F(1,465) = 1,730, p = 0,178, r = 0,086$
- sovraštvo: $F(1,465) = 0,830, p = 0,437, r = 0,060$

REZULTATI: ŽENSKE



Slika 3. Povprečni dosežki skupin na podlestvicah agresivnosti (ženske)

- fizična agresivnost: $F(1,301) = 1,006, p = 0,367, r = 0,081$
- besedna agresivnost: $F(1,301) = 0,810, p = 0,446, r = 0,073$
- jeza: $F(1,301) = 3,457, p = 0,032, r = 0,150$
 - post hoc (Gabrielov postopek): skupina nosečnosti in kontrolna skupina 2, $p = 0,027$
- sovraštvo: $F(1,301) = 1,170, p = 0,312, r = 0,088$

DISKUSIJA

- ni značilnih razlik v izraženosti potez agresivnosti...
- ... razen pri ženskah – podlestvica jeze: v skupini nosečnosti med vojno manj izražena kot v skupini po vojni
- fetus ni enako ranljiv za zunanje vplive v vseh treh semestrih
- možni moderatorski učinki genotipa med prenatalnim stresom in agresivnostjo
 - DRD4 alel kot moderator med prenatalnim stresom in agresivnostjo (15)
- je 10-dnevna vojna ustrezen stresor?
- materina percepcija vojne kot stresorja
- možni drugi stresni dogodki med nosečnostjo
- različna izpostavljenost (geografska spremenljivka)

ZAKLJUČKI

nadaljevanje študije:

- povezava med prenatalnim stresom in ranljivostjo za druge motnje v duševnem zdravju (TEMPS-A, CAD)
 - povezovanje podatkov z androloškimi podatki o reproduktivnem zdravju
 - analize po trimesečjih nosečnosti za skupino, izpostavljeno stresorju
-
- pomembno za razumevanje mehanizmov in učinkov prenatalnega stresa na vedenjske poteze → možnost za intervencije za obvladovanje prenatalnega stresa za noseče matere, izpostavljene stresu

LITERATURA

- Alink, L. R., van Ijzendoorn, M. H., Bakermans-Kranenburg, M. J., Mesman, J., Juffer, F., in Koot, H. M. (2008). Cortisol and externalizing behavior in children and adolescents: mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. *Developmental Psychobiology*, 50, 427-50.
- Bergman, K., Sarkar, P., O'Connor, T. G., Modi, N., in Glover, V. (2007). Maternal stress during pregnancy predicts cognitive ability and fearfulness in infancy. *Journal of American Academy of Child and Adolescent Psychiatry*, 46, 1454-63.
- Buchmann, A. F., Zohsel, K., Blomeyer, D., in Hohm, E. (2014). Interaction between prenatal stress and dopamine D4 receptor genotype in predicting aggression and cortisol levels in young adults. *Psychopharmacology*, 231, 3089-97.
- Buss, A. H., in Perry, M. (1992). The aggression questionnaire. *Journal of personality and social psychology*, 63(3), 452.
- Cotrell, E. C., in Seckl, J. R. (2009). Prenatal stress, glucocorticoids and the programming of adult disease. *Frontiers in Behavioral Neuroscience*, 3(19). doi: 10.3389/neuro.08.019.2009
- Dancause, K. N., Laplante, D. P., Oremus, C., Fraser, S., Brunet, A., in King, S. (2011). Disaster-related prenatal maternal stress influences birth outcomes: Project Ice Storm. *Early Human Development*, 87, 813-20.
- de Bruijn, A. T. C. E., van Bakel, H. J. A., in van Baar, A. L. (2009). Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Human Development*, 85, 319-24.
- Field, T., in Diego, M. (2008). Cortisol: the culprit prenatal stress variable. *International Journal of Neuroscience*, 118(8), 1181-205.
- Glover, V. (2011). Annual Research Review: Prenatal stress and the origins of psychopathology : an evolutionary perspective. *Journal of Child Psychology and Psychoatry*, 52(4), 356-67.
- Gowin, J. L., Green, C. E., Alcom, J. L. III., Swann, A. C., Moeller, F. G., Lane, S. D. (2013). The role of cortisol and psychopathy in the cycle of violence. *Psychopharmacology (Berlin)*, 227, 661-72.
- Graignic-Philippe, R., Dayan, J., Chokron, S., Jacquet, A. Y., in Tordjman, S. (2014). Effects of prenatal stress on fetal and child development: a critical literature review. *Neuroscience & Biobehavioral Reviews*, 43, 137-62.
- Harville, E., Xiong, X., in Buekens, P. (2010). Disasters and perinatal health: a systematic review. *Obstetrical & Gynecological Survey*, 65, 713-28.
- Hay, D. F., Pawlby, S., Waters, C. S., Perra, O., in Sharp, D. (2010). Mothers' antenatal depression and their children's antisocial outcomes. *Child Development*, 81, 149-65.
- Huizink, A. C., Robles de Medina, P. G., Mulder E. J., Visser, G. H., in Buitelaar, J. K. (2003). Stress during pregnancy is associated with developmental outcome in infancy. *Journal of Child Psychology and Psychiatry*, 44, 810-18.
- Khashan, A., S., Abel, K. M., McNamee, R., Pedersen, M. G., Webb, R. T., Baker, P. N., idr. (2008). Higher risk of offspring schizophrenia following antenatal maternal exposure to severe adverse life events. *Archives of general psychiatry*, 65, 146-52.
- Platje, E., Jansen, L. M., Raine, A., Branje, S. J., Doreleijers, T. A., de Vries-Bouw, M., Popma, A., van Lier, P. A., Koot, H. M., Meeus, W. H., in Vermeiren, R. R. (2013). Longitudinal associations in adolescence between cortisol and persistend aggressive or rule-breaking behaviour. *Biological Psychology*, 93, 132-7.
- Popma, A., Vermeiren, R., Geluk, C. A., Rinne, T., van den Brink, W., Knol, D. L., Jansen, L. M., van Engeland, H., in Doreleijers, T. A. (2007). Cortison moderates the relationship between testosterone and aggression in delinquent male adolescents. *Biological Psychiatry*, 61, 405-11.
- Poustka, L., Maras, A., Hohm, E., Fellingner, J., Holtmann, M., Banaschewski, T., Lewicka, S., Schmidt, M. H., Esser, G., in Laucht, M. (2010). Negative association between plasma cortisol levels and aggression in a high-risk community sample of adolescents. *Journal of Neural Transmission*, 117, 621-7.
- Robinson, M., Mattes, E., Oddy, W. H., Pennel, C. E., van Eekelen, A., McLean, N. J., idr. (2011). Prenatal stress and risk of behavioral morbidity from age 2 to 14 years: the influence of the number, type, and timing of stressful life events. *Development and Psychopathology*, 23, 507-20.
- Weinstock, M. (2008). The long-term behavioural consequences of prenatal stress. *Neuroscience & Biobehavioral Reviews*, 32, 1073-86.
- Weinstock, M. (2007). Gender differences in the effects of prenatal stress on brain development and behaviour. *Neurochemical Research*, 32, 1730-40.

HVALA ZA VAŠO POZORNOST!



urska.smrke@zrc-sazu.si

<http://dmi.zrc-sazu.si/sl#v>

Raziskavo sofinancira Javna agencija za raziskovalno dejavnost Republike Slovenije, št. projekta J3-6801.