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Seventh Framework Programme

ACTION

ACTION: Aggression in Children: Unraveling gene-environment interplay to inform Treatment and InterventiON strategies

Grant Agreement N. **602768**

D 4.1 Identify and replicate ‘pure’ environmental risks that have their effects on the development of aggression independent of genetics

Date of deliverable: 01/06/17
Actual submission date: 07/06/17
Version: 1.0

Topic(s): HEALTH.2013.2.2.1-3 - Paediatric conduct disorders characterised by aggressive traits and/or social impairment: from preclinical research to treatment
Call for proposal: FP7-HEALTH-2013-INNOVATION-1
Funding scheme: CP-FP - Small or medium-scale focused research project
Start date of the Project: 1st June 2014. Duration: 60 months
Coordinator: VU University Amsterdam, Department of Biological Psychology

Project funded by the European Commission under the Seventh Framework Programme		
Deliverable’s Restriction Level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission services)	
RE	Restricted to a group specified by the consortium (including the Commission services)	
CO	Confidential, only for members of the consortium (including the Commission)	

D4.1

Identify and replicate 'pure' environmental risks that have their effects on the development of aggression independent of genetics

Responsible

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Summary: The following report outlines progress toward identifying and replicating new measures of environmental risk

Keywords: Aggression, adolescence, non-shared environment, monozygotic twins.


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1 THEORETICAL BACKGROUND

Aggression inflicts a substantial financial and societal burden, calling for novel preventative approaches to alleviate its negative impact. The aetiology of childhood aggression represents a complex interaction between genetic and environmental sources of variation. Powerful designs aimed at disentangling this complex relationship are needed in order to identify 'pure' environmental influences on aggression, independent of genetic effects, which can inform causative targets and guide the development of novel strategies. We sought to elucidate the most prominent environmental risk factors that replicate across comprehensive longitudinal cohorts. This report details the extensive mega-analyses of ACTION twin datasets conducted to fulfill this aim. Specifically, we detail 1) Analyses that exploit the multidimensional nature of risk exposure, to identify environmental risk factors spanning early and late adolescent life; 2) Progress on applying results from our multidimensional analyses to identifying pairs discordant for adolescent aggression and updates on in-depth interviews to gain new insight in causes of discordance; 3) Results from analyses reflecting a persistent and robust effect of maternal smoking during pregnancy on aggression, replicated across four ACTION cohorts.

2 BACKGROUND TO STUDY 1

Studies investigating the factors predicting differences in aggression between adolescents have mostly focused on examining the role of few measures often restricted to the same sphere (e.g. school environment or home environment). However, adolescents' aggressive behaviour is likely to be influenced by several risk factors spanning multiple areas of their lives. The first aim of the present study is to identify the combined predictive power of multiple risk factors to variation in aggression during adolescence. The second aim is to quantify the degree of genetic and environmental influence on the association between multidimensional risk scores (MRS) and aggression. Most pertinent to this aim is identifying the degree to which environmental sources of variation that contribute to the compound effect of multiple risk factors stem from those experiences shared between individuals growing up within the same home (shared environment) and from those experiences unique to the individual (non-shared environment). Results from these analyses will form the basis of exploratory interviews with a small subset of MZ pairs discordant for aggression, which is discussed further in the background to study 2.

2.1 METHOD

The initial sample included 5,635 twin pairs, members of the Twins Early Development Study, conducted as a prelude to obtaining data from the other ACTION samples. Data were collected on environmental risks and aggression when the twins were 12 and 16 years old. Beta-weighted MRS were calculated separately for aggression at age 12 and 16. MRS included multiple measures of home and school environment and peer relationships. The twin method was applied to explore the aetiology of the environmental risks with aggression.

2.2 RESULTS

MRS predicted a similar portion of variance in concurrent aggression at both ages 12 and 16 ($R^2 = .10$ and $R^2 = .11$, respectively). The aetiology of the association between MRS and aggression differed between early and late adolescence. While shared environment explained the main proportion of covariance at 12 (51%), genetic factors were the main source of covariance at 16 (50%). Although non-shared environment was the main factor in the aetiology of aggression at 16 ($e^2 = 72\%$), it was only minimally implicated in the overlap between MRS and aggression.

2.3 CONCLUSION

The risk factors of aggression span multiple domains of adolescents' lives. Although MRS predicted a significant portion of variance, the effect is modest, emphasising the need for future research to identify additional risk factors. The observed lack of nonshared environmental overlap with aggression suggests that nonshared environment may be highly idiosyncratic—in-depth follow-up interviews with a subset of the TEDS study will investigate this further. In line with the collaborative ethos of ACTION, we are awaiting data from other ACTION samples in order to corroborate these findings across multiple cohorts.

3 BACKGROUND TO STUDY 2

Converging evidence demonstrates that the most influential environmental influences on differences in aggression are those that are individual-specific, or non-shared. Nonetheless, non-shared environmental influences to discordance in aggression are poorly understood. The current study offers a novel approach to generating new, testable hypotheses for sources of variation in early adult aggression. Specifically, we capitalize on the powerful monozygotic (MZ) twin differences design. Because MZ twins share 100% of their genetic material and 100% of their shared environment, any differences between them must be accounted for by the non-shared environment (including measurement error). Thus, the MZ twin difference design provides an unbiased estimate of ‘pure’ environmental sources of variation on a trait. Results from study 1 demonstrate that risk factors for aggression span multiple domains of adolescents’ lives, we expand on these analyses to identify the most pertinent aspects of the home, school and friends in contributing to early adult aggression.

As part of study 2, we are currently conducting in-depth interviews with MZ twins who are extremely discordant for aggression. Twin pairs are being interviewed with the aim of identifying the environmental differences between them that may contribute to differences in their early adult aggression. This method has the unique advantage of gaining insight in ‘pure’ environmental influences due to the fact that the twins are genetically identical. It also offers an unprecedented opportunity to generate novel hypotheses of the non-shared environmental factors most pertinent to twin discordance.

We aim to address the following objectives:


- Understand twin perceptions of discordance for aggression
- Test for the relationship between discordance and multiple domains
 - Home
 - Friends
 - School
- Probe for the environmental factors most commonly ascribed to twin pair discordance
- Generate new hypotheses for sources of non-shared environmental influence which can be tested empirically within ACTION

3.1 METHOD

Twins were identified and approached to take part in the interview study on the basis of their zygosity and response to self-report measures of aggression, collected when they were age 16.

Zygoty was assessed by a parent-reported questionnaire of physical similarity, which is over 95% accurate when compared to DNA testing. For cases where zygosity was unclear from this questionnaire, DNA testing was conducted. Aggression was based on a self-report questionnaire administered to the wider TEDS sample, at the 16 year data collection.

New measures were developed for the semi-structured interview, designed to elicit responses on the causes of twin pair discordance for aggression in early adolescence. Based on results from study 1 (described above) we focused on environmental influences across multiple domains, specifically the home, school and friendship environment. Questions were designed to probe reasons for discordance, and whether participants would ascribe these sources of discordance to differences between themselves and their twin in their home life, school, or friendships. Free-

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response questionnaire data will be gathered from participating twins via telephone interview, which will be recorded. Following the interview, data will be transcribed and analysed to identify common themes.

3.11 PROGRESS UPDATE

We have made good progress on identifying the particular non-shared environmental sources of variation most pertinent to childhood aggression.

Specifically, we have developed the script template for the semi-structured interview as well as created the email invitation and information sheet (see Appendix) which will be sent out to the discordant twin pairs. We have also identified MZ twin pairs extremely discordant for aggression based on the following criteria:

- Presence of contact details
- Aggression data present at age 16
- Zygosity known
- Discordance in aggression of at least 1.5 standard deviations between pairs

3.11.1 Planned course of action

We are preparing e-mail invitations which will be sent out to the discordant MZ twin pairs from TEDS. Following scheduling, two research students working from the ACTION grant will conduct the semi-structured interviews. Interviews will then be transcribed and analysed to identify common themes across twin pairs, emphasizing the multi-dimensional facet of aggression (i.e., to what extent twins ascribed their discordance to differences in their experience of their home, school and peers). These data will be written up in a manuscript together with results from study 1 in order to inform future research on 'pure' environmental sources of variation in aggression.

4 BACKGROUND TO STUDY 3

Identifying reliable environmental risk factors for childhood aggression that replicate across longitudinal cohorts is essential for efforts to alleviate the societal burden associated with these behavioural problems. Early perinatal factors have been linked to children's externalising problems, in particular maternal smoking during pregnancy (SDP). The mechanisms underlying this association remain poorly understood and research to date has been largely underpowered. It has been argued that socio-demographic factors, such as maternal age and education, are likely to account for the association between SDP and later behavioural outcomes. The present study explores how perinatal risk factors contribute to individual differences in aggression throughout late childhood and adolescence, focusing on the independent effect of SDP.

4.1 METHOD

Participants were members of four developmental twin samples from ACTION –the Twins Early Development Study (TEDS), the Netherlands Twins Registry (NTR), the Childhood and Adolescent Twin Study of Sweden (CATSS) and the Finnish Twin Cohort Study (FT12). Data from more than 45,000 randomly selected members of twin pairs were available. A harmonised measure of aggression was created for every collection wave (ages 9-10; 12; 14-15 and 16-18).

4.2 RESULTS

SDP predicted aggressive behaviour in late childhood and adolescence, independently from early perinatal factors. A meta-analysis across the four samples found the independent effect of SDP to be 0.3% ($r = .06$). All other perinatal factors combined explained 1.25% of the variance ($r = .11$). The effects remained consistent when analyses were performed on co-twins and for males and females separately.

2.4 CONCLUSIONS

SDP consistently predicts aggression in adolescence, beyond co-occurring socio-demographic and perinatal measures and across four developmental twin samples. The ability to identify a consistent effect of an early environmental influence on behavioural outcomes 15 years later, represents an important benefit of collaborative projects to further knowledge on socially relevant behaviours and outcomes. We are now collecting data on paternal smoking behaviour to test the extent to which this identified risk factor is specific to intrauterine exposure or whether it extends to the presence of any smoking within the household.

5 GENERAL CONCLUSIONS

The extensive analyses detailed in this report reflect collaborative efforts to identify pure environmental risk factors that affect the development of aggression. The following conclusions can be drawn from these findings

- Non-shared environmental sources of influence on the aetiology of early adult aggression are substantial, but may reflect more idiosyncratic experiences rather than systematic insults that generalise to groups
- MZ differences designs offer novel approaches to generate new data driven hypotheses for 'pure' environmental risk factors for aggression
- Maternal smoking reflects a persistent, albeit modest, risk factor for later aggression—posing a feasible target for early preventative intervention



TEDS RESEARCH CENTRE

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<Date>

Dear, <Twin 1 forename> and <Twin 2 forename>,

We are particularly interested in some of the differences in your temperament you described when you were 16 and would appreciate the chance to explore them further with you both in our new study. We are inviting 10 families, including yours, to take part in a telephone interview study of differences between identical twins and hope you will agree to participate.

To find out more about what taking part involves please read the information sheet provided. If you decide that you would like to take part please provide your consent electronically. One of our researchers will then call you directly to arrange a time that suits you for a telephone interview to take place and to answer any questions you may have about the study. To say thank you for your participation we will send you a £30 Love2Shop voucher.

Yours sincerely

Professor Robert Plomin and the TEDS team

<Twin ID>

The logo for ACTION, featuring the word "ACTION" in blue capital letters followed by a black and white yin-yang symbol.	Do.o Deliverable name
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Understanding pupil's temperament in late adolescence and early adulthood

We would like to invite you to participate in this original research project. You should only participate if you want to. If you do take part you are free to withdraw at any point without giving a reason. Your decision not to take part in this study will not affect your involvement with TEDS. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. If you have any questions then please feel free to contact us by email or on our Freephone number.

What is the study about?

You may remember completing a questionnaire when you were aged 16 about the ways in which your twins differ from each other. That questionnaire was the first stage in our exploration of the experiences that influence young people's decisions, achievements and general well-being as they complete their compulsory education. The next stage in the study is to talk to families with identical twins who are particularly different from each other in one or more ways, and to ask for your thoughts about how to explain these differences.

Who have we asked to participate?

We will invite approximately 10 families to participate in this study. These are families with identical twins who appear to be particularly different from one another in one or more ways. Other than being identical twins showing at least one strong difference there are no restrictions on taking part in this study.

How do we take part?

If you consent to taking part in this study we will phone you to arrange a time for a telephone interview. During the interview we will ask questions about the differences you described and your explanations for how these differences might have come about. Each interview is likely to last for between 10 minutes and half an hour. During the interview if there are any questions that you would prefer not to answer then please feel free to tell the interviewer that you would like to move on.

Sample questions include:

- What role do you think your friends played in your temperament at age 16?
- How do you think your school contributed to your temperament at age 16?

Interviews will be recorded and then transcribed. The recordings will be deleted upon transcription and the transcription will be stored anonymously on a secure server.

Are there any risks involved in participating?


The research entails no risks beyond those of ordinary life.

Are there any benefits involved in participating?

At the conclusion of the project we will publish our most significant findings on the TEDS website so that you can access them (www.teds.ac.uk). We will also use the website to alert you to any research publications we have generated from the project.

As a token of our appreciation we will send you and your twin a £30 gift voucher. You will not, however, benefit financially from the research in any other respect.

How will we maintain your privacy and confidentiality?

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All information we receive from your family is strictly confidential. You are identified only by a number in the study datasets. Identifiable data will only be accessed by authorised members of the TEDS team and stored in a separate secure location. The data your family provides will be kept for a minimum of 10 years after completion of the TEDS study, as recommended by the Medical Research Council (MRC). TEDS data are sometimes shared with other researchers, but only after removing identifying information about the participants. We will not pass your family's information on to any other organisations. The data may be retained for use in future studies subject to further ethical approval.

Who is organising the research?

The research is being organised by Professor Robert Plomin of the TEDS study.

Do you have to take part?

It is up to you to decide whether or not to take part. If you do take part, you are free to withdraw yourself and your data at any time without giving a reason. Your decision not to take part in this study will not affect your future involvement with TEDS.

Queries?

If you have any questions do not hesitate to call us on our freephone line 0800 317 029, or email us at teds-project@kcl.ac.uk.

Thank you from all at TEDS!