

## **MANUSCRIPT FACT SHEET: Genetic vulnerability to bullying**

An international research team led by Karen Sugden, at King's College London and Duke University reports new evidence that children who had experienced victimization by bullies were more likely to develop emotional problems at 12 years old, but only if they had one version of a genetic polymorphism in the serotonin transporter gene. Bullied children having a different version of the same gene developed fewer emotional problems. This fact sheet summarises the report.

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### **TITLE:**

Serotonin Transporter Gene Moderates the Development of Emotional Problems Among Children Following Bullying Victimization

### **THE FINDING:**

Research into the effects on bullying victimization has indicated that bullied children have an elevated risk of developing emotional problems. Our research asked why only some children who are the victims of bullies seem to be vulnerable to emotional problems whilst others are not. Evidence from a longitudinal-prospective study of 2,017 12-year old British children showed that the relationship between bullying victimization and emotional problems depends on the victim's genotype on the serotonin transporter (*5-HTT*) gene. This region comes in two versions, the "short" versus the "long", and each person inherits two copies, one from each parent (a genotype). The study revealed that the "short/short" genotype conferred vulnerability to bullying victimization.

Twice as many frequently bullied short/short genotype children had clinically-relevant levels of emotional problems when compared to frequently bullied long/long-genotype children (31.7% vs. 15.1).

Because children who start off with higher levels of emotional problems might have a greater chance of being the targets of bullies or a genetic pre-disposition to emotional problems, we checked to see if the interaction between the gene and bullying predicted *increases* in emotional problems between age 5 (before the bullying was reported) and age 12 (after bullying). We found that short/short genotype children remained at greater risk of developing emotional problems after frequent bullying victimization than other children, regardless of their initial level of emotional problems at age 5.

We also compared emotional problems in twins who share both their genotype *and* family environment, but who differed in that one twin was bullied but their twin was not. In short/short twin pairs, the bullied twin had higher levels of emotional problems than their non-bullied co-twin.

Our findings emphasize that there is a biological basis that underlies children's vulnerability to the harmful effects of bullying. This information may help suggest intervention strategies for those children most at risk from the negative effects of bullying victimization.

### **FEATURES OF THE STUDY THAT SUPPORT THE FINDING:**

**(a)** Children who had the at-risk short/short genotype and were bullied were viewed as having worse emotional problems by both their mothers and teachers. i.e., the finding was not based merely on one person's report.

**(b)** A child who has emotional problems might overstate their bullying experience because they perceive events more negatively than others, which can lead to inaccurate measures. We asked the

mothers and teachers about the child's emotional problems, as well as the child themselves about their bullying victimization, to make as unbiased a measure as possible.

**(c)** Scientists ask, might people's genetic makeup lead them to be bullied? Tests that showed the bullied twins developed more emotional problems from ages 5-12 years ruled out this possibility.

**(d)** Scientists might also ask, could something in a child's home environment make them more susceptible or resilient to emotional problems after bullying victimization? If so, then the genetic moderation might be a reflection of these 'shared' environmental factors that we did not measure. Tests of emotional problem scores in twins who shared their genotype and home environment, but differed on bullying victimization ruled out this possibility.

## **DISCUSSION POINTS:**

**(a)** This study does not suggest that bullying victimization alone is a major cause of emotional problems. The effect applies to few children, and thus would not be expected to raise rates of mental illness in the population.

**(b)** This study is important because it reiterates that serotonin transporter gene variation is important in modulating the response to stressful events. This finding has been reported before in adults who experienced stress, but it remains controversial. We used recent important discoveries in other fields such as neuroscience to direct our hypotheses, and we found the connection because we looked at a specific, well-defined stressful event (bullying victimization). We recommend that researchers should aim to define environmental measures as precisely as possible, and make full and profitable use of a wide range sources to direct their research into gene environment interactions

**(c)** The children in this study were tested at 12 years old; we do not yet know what the future burden of childhood bullying might be for these children in terms of adult mental health. We will be following these children through to adulthood when such questions could be answered.

**(d)** This is not a case of a rare genetic mutation that is the major cause of a disease. Instead, the *5-HTT* "polymorphism" is a naturally occurring variation in the genetic sequence of DNA. Its two variations are both common among humans, 17.5% of children carry two copies of the short version, so it is too common to be a direct cause of disease. Common genetic variants like this one probably act only in response to environmental conditions.

## **SUPPORTING DETAILS:**

### **Participants**

Participants were 1,116 pairs of twins born in 1994 and 1995 in England and Wales. This birth cohort was initially assessed at age 5, and has been followed up at ages 7, 10 and most recently at 12 years, when more than 90% of the cohort (2,017 individual children) took part. The twins pairs were both monozygotic (identical; 55%) and dizygotic (fraternal; 45%), and all the pairs were the same sex.

### **The Serotonin transporter (5-HTT) gene**

The gene we chose to study is called the serotonin transporter gene (*5-HTT*). Specifically, we analyzed a well-studied polymorphism known as the serotonin transporter linked polymorphic region (*5-HTTLPR*) within the gene's promoter. This regulatory region gives rise to two common forms of the gene (known as 'alleles') of which the "short" allele is associated with lower efficiency of the gene compared with the "long" allele. We chose to study it for 6 reasons. First, lower efficiency of the gene has been linked to dysregulated serotonergic functioning and emotional problems. Second, functional magnetic resonance imaging (fMRI) studies have shown that the short allele is associated with exaggerated response to threat in a key brain region known to be involved in behavioural arousal. Third, short-carriers are more likely pick up and retain fear of stimuli associated with threat. Fourth, short/short carriers have higher and longer-lasting cortisol levels after stress exposure (cortisol is a hormone is released in response to stress). Fifth, long/long carriers more frequently avoid looking at threatening material and focus on the positive, suggesting that they are protected from stress by "looking on the bright side of life". Sixth, Research with rhesus macaques (a non-human primate) has

shown that short-carrying monkeys were more likely to be threatened by and to avoid more dominant monkeys, suggesting that short-carriers may be more sensitive to the threat of confrontation in the context of power imbalance (such as that experienced when bullied).

Each person inherits two copies of the 5-HTTLPR, one from their mother and one from their father. So a person has one of three possible combinations. In the birth cohort we studied, 352 individuals (17.5% of the sample) had two copies of the stress-sensitive version of the gene (short/short), 992 individuals (49.2%) had one stress-sensitive and one alternate copy (short/long), and 673 individuals (33.4%) had two copies of the alternate gene (long/long). These percentages match the rates of this genetic polymorphism in the Caucasian population. Boys and girls do not differ on this gene, and neither do identical and fraternal twins.

### **Bullying victimization**

Bullying victimization was assessed during private interviews with the children during home visits when they were age 12 years. We explained to them that someone is being bullied when another child (1) says mean and hurtful things, makes fun or calls a person mean and hurtful names; 2) completely ignores or excludes someone from their group of friends or leaves them out of things on purpose; 3) hits, kicks, or shoves a person, or locks them in a room; 4) tells lies or spreads rumors about them; and 5) other hurtful things like these. We call it bullying when these things happen often, and it is difficult for the person being bullied to stop it happening. We do not call it bullying when it is done in a friendly or playful way. Children indicated whether they had been bullied by another child "never", "sometimes", or "a lot". When a child reported being bullied, the interviewer asked the child to describe what happened. Notes taken by the interviewers were later checked by an independent rater to verify that the events described by the child relate to instances of bullying. 11.4% of the children reported that they were frequently bullied, 41.8% occasionally bullied and 46.8% were never bullied by age 12.

### **Emotional problems**

Emotional problems were assessed by administering a standard questionnaire about the twin's emotional behaviour to both the twins' mother and teacher at age 5 years and again at age 12 years. Indicators of emotional problems using these questionnaires include such things as the child crying a lot, being withdrawn, not getting involved with others and worrying. We combined the mother and teacher reports at each age, as we have done in our other reports in our research program on bullying.

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