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Review

THE CORRELATION BETWEEN GENETICS AND SUICIDAL BEHAVIORS: A CHALLENGE OF LITERATURE

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SUMMARY

Suicide and suicidal behaviors seem to have a heritable component, and evidences from adoption, twins and families studies underline observations that greater familial suicidal behavior correlates with earlier onset and higher risk in offspring, supporting the presence of a genetic component. In this paper we report data from the literature, highlighting the scientific relevance of research in important topic as suicidal behaviours.

Key words: *suicide - suicidal behaviors - genetic influence - genetic studies*

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INRODUCTION

Suicide is a complex phenomenon influenced by various biological and psychosocial factors. It involves a specific mental state that both motivates and accompanies this extreme and final act. It lies at the end of a series of forms commonly referred to as suicidal behaviours (SB) that include suicide attempts and suicidal ideas: a suicide attempt is a potentially self-injurious behavior with a nonfatal outcome, indicating some level of intent to die, but may not result in injuries. Suicide completers are considered a more homogeneous group than suicide attempters, with both groups sharing only some underlying etiological and neurobiological mechanisms (Costanza et al. 2014). Suicidal behaviors have been shown to run in families and are linked to biological traits and risk factors that are not necessarily shared with the associated psychiatric disorders (Punzi et al. 2022). Here, we analyzed the available literature considering the correlation between genetics and suicidal behaviors.

SIGNALING MOLECULES WITH GENETIC IMPACT IN SUICIDAL BEHAVIORS

Neurotransmitters

Among neurotransmitters, impaired expression of GABAergic genes has been identified in individuals who have completed suicide (Costanza et al. 2014). Several GABA receptor subunits, including GABA-A receptor-associated protein like 1 (GABARAPL1) and the GABA transporter (SLC6A1), showed altered gene expression patterns in the prefrontal cortex (PFC) and limbic brain regions of suicide victims (Fiori & Turecki 2010, Kim et al. 2007). Another study pointed out that the density of AMPA receptors, another type of glutamate receptor, might be increased in the caudate nucleus of individuals who have died by suicide (Noga et al. 1997). Notably, adrenergic transmission was suggested to play a role in suicide, evidenced by decreased noradrenaline levels in the brainstem and increased densities of α2-adrenergic receptors due to noradrenaline deficit (Bondy et al. 2006). On the other hand, alterations in α2-adrenergic signaling pathways have been observed in the frontal cortex of depressed suicide victims (Valdizán et al. 2010). In contrast, no significant differences in dopamine (DA) concentrations were found in cortical and subcortical regions between suicide victims and controls; the presence of dopamine D2 receptors has been proposed to increase the risk of suicidal behavior in individuals with a familial history of alcoholism. Regarding opioids, two different studies that performed quantitative autoradiography have found higher densities of μ-opioid receptors in the frontal and temporal cortex of younger individuals who completed suicide (Gross-Isseroff et al. 1990, Gabilondo et al. 1995).

Serotonin (5-HT) is believed to significantly influence the neurobiology underlying SB. Alterations in the 5-HT system are known components of the neurobiological predisposition to suicide. Abnormalities have been observed in the hypothalamus, brainstem and prefrontal cortex (PFC) of suicide victims, particularly in the ventral prefrontal cortex (VPFC) (Mann 2003). In detail, low levels of 5-hydroxyindoleacetic acid (5-HIAA), a major serotonin metabolite in cerebrospinal fluid, have been linked to violent suicide attempts, suggesting it may serve as a specific predictor for suicidal behavior (Asberg et al. 1979). It has been hypothesized that this biochemical trait can be assumed as a predictor of suicide attempts and their completion since that low post-mortem levels of 5-HIAA have been found in suicide victims (Costanza et al. 2014). Molecular genetic studies have focused on serotonin-related genes like tryptophan hydroxylase 1 and 2 (TPH1 and

TPH2) and the serotonin transporter gene (5-HTT; SLC6A4). Regarding to TPH1, different polymorphisms have been associated with suicide attempt, but none have been implicated in suicide completion (Bondy et al. 2006). Variants in the promoter region of TPH2, particularly SNIP rs-10748185, had a considerable effect on TPH2 mRNAa level that was found to be increased in the VPFC of suicide completers (Perroud et al. 2010). Supporting this data, another study has identified higher level of TPH2 mRNAa in the raphe nuclei and in the DLPFC of suicide victims (Bach-Mizrachi et al. 2006). Furthermore, alterations in serotonin receptor (5-HTR) expression, particularly upregulation of 5-HTR-1A and 5-HTR-2A in the prefrontal cortex of suicide victims, suggest a compensatory response to reduced serotonin activity (Oquendo et al. 2006). These findings highlight the complex interplay of serotonin system dysregulation and genetic factors in the predisposition to suicidal behavior, warranting further investigation into their roles and potential as biomarkers for suicide risk.

Hypothalamic-pituitary-adrenal axis (HPA)

The HPA axis is the primary biological system governing human stress responses, and its dysfunctions have been studied in depressed and suicidal individuals (Costanza et al. 2014). Cortisol nonsuppression in the dexamethasone suppression test (DST) is strongly associated with completed suicides, making it a potential predictor for suicide in depressed patients (Coryell and Schlesser 2001). The hyperactivity of corticotrophin-releasing hormone (CRH) in the hypothalamic paraventricular nucleus was identified by postmortem studies as a common characteristic of depressed and suicidal individuals (Turecki et al. 2012) showing increased CRH neuron counts and CRH mRNA levels. Increased pro-opiomelanocortin mRNA in the pituitary gland and reduced CRH binding sites in the prefrontal cortex were also observed in suicide victims (Nemeroff et al. 1988). Furthermore, depressed suicides exhibit elevated CRH immunoreactivity, increased CRH mRNA levels, and reduced CRH receptor type 1 (CRH1) levels, potentially due to elevated CRH levels (Austin et al. 2003; Merali et al. 2006). Epigenetic mechanisms have also been considered in molecular genetic studies of suicide. In fact, DNA methylation of the NR3C1 promoter of the glucocorticoid receptor (GR) gene, was observed in the hippocampus of suicide victims with childhood abuse histories, resulting in decreased GR mRNA and GR 1F splice variant transcripts (McGowan et al. 2009). This epigenetic modification leads to HPA axis hyperactivity and a failure to respond to glucocorticoid feedback.

Neurotrophic factors

Studies of suicide completers, mostly diagnosed with major depression, show downregulation of brain-derived neurotrophic factor (BDNF) and tropomyosin-related kinase B (TrkB) in various brain regions (Pandey et al. 2008). Decreased BDNF levels were found in the hippocampus and VPFC, and reduced neurotrophin-3 (NT-3) in the hippocampus of untreated suicide victims (Karege et al. 2005). FGFR3 and FGFR2, receptors of FGF, were also downregulated in the prefrontal cortex and other brain regions of suicide victims (Ernst et al. 2009a). The same genes were analyzed in epigenetic studies showing that stressed rats had hypermethylation of BDNF promoter exons, which was also found in the Wernicke's area of suicide completers (Keller et al. 2010). On the other hand, a variant of TrkB (TrkB-T1) specific to astroglial cells was downregulated in the orbital frontal cortex of suicide completers and associated with promoter methylation (Ernst et al. 2009b). This methylation was specific to the prefrontal cortex and not observed in Wernicke's area or the cerebellum.

Protein kinases and signaling molecules

Several signaling molecules and kinases have been involved in suicide. Among them, protein kinase Akt decreased and glycogen synthase kinase-3β increased in depressed suicide victims (Karege et al. 2007). Other studies highlight that the P11 protein (S100A10), which regulates various cellular processes and is linked to depression, was significantly lower in the blood cells of suicide attempters and in the prefrontal cortex of suicide completers (Zhang et al. 2011). These pathways interact with neurotransmitter systems and genes associated with suicide, such as the activation of transcription factors by protein kinase C (PKC) leading to BDNF transcription (Costanza et al. 2014).

Polyamines

Alterations in polyamines have been linked to psychopathology in both humans and animals. For istance, in suicide completers with or without major depression, the expression of spermidine/spermine N1-acetyltransferase 1 (SSAT) was significantly downergulated in VPFC and other brain regions (Klempan et al. 2009, Sequeira et al. 2006). In addition, several single nucleotide polymorphisms (SNPs) in SSAT have been associated with suicide in French Canadians, with specific haplotypes modifying its expression and DNA methylation at the SSAT gene promoter was negatively correlated with its expression in suicide completers (Fiori & Turecki 2010).

ADOPTION, TWINS AND FAMILY STUDIES

Adoption studies

Genetic basis of suicide and suicidal behaviors have been analyzed in adoption studies, by two major works. The first one compared suicide rates among biological

and adoptive relatives of adoptees who committed suicide with those in a matched living adoptee control group. The study found a six-fold higher rate of suicide among biological relatives of suicide adoptees, with no suicides among adoptive relatives, suggesting a genetic rather than environmental effect. This increased rate was observed regardless of whether the adoptees were psychiatric patients (Schulsinger et el. 1979). The second study was conducted by Wender et al. using the Danish adoption registry and focusing on mood disorders. They found a 15-fold excess of suicide among the relatives of mood-disordered adoptees, supporting the role of mood disorders in the genetics of suicide. However, the highest suicide rates were in relatives of adoptees diagnosed with "affective reaction" (impulsive-unstable or Cluster B personality disorders), suggesting a familial link between impulsive aggression and suicide, independent of mood disorders (Wender et al. 1986).

Twins studies

A study of Roy et al. reported an even higher concordance rate for suicide attempts in the surviving monozygotic (MZ) twin after the co-twin's suicide (38% vs. 0%), suggesting that the clinical phenotype for concordance includes both completed suicides and suicide attempts (Roy et al. 1995). Another study, reviewed published twin case reports on suicide and found higher concordance rates for suicide and suicidal behavior in MZ twins compared to dizygotic (DZ) twins (14.9% vs. 0.7%, and 23.0% vs. 0.7% respectively) (Roy and Segal 2001). These findings, based on case series, might not represent all twins who experienced suicide; the higher concordance rate in MZ twins was not due to greater bereavement reactions, as the risk of suicide attempts after a non-suicide death of a co-twin was similar in both MZ and DZ twins (1.4% vs. 3.3%) (Brent & Mann 2005).

Three twin studies showed that familial transmission of suicidal behavior cannot be explained solely by the transmission of other psychopathologies. While there was some overlap between the heritability of suicidal ideation and actual suicidal behavior, a distinct heritable component of actual suicidal behavior has been demonstrated. Statham et al. studied 5,995 Australian twins and found that a MZ twin attempting suicide increased the risk of a suicide attempt in the co-twin by 17.5 times. The concordance rate for serious suicidal behavior was much higher in MZ twins (23.1%) compared to DZ twins (0%). After controlling for other risk factors, a family history of suicide attempts still conveyed a 3.8-fold increased risk. Heritability estimates for suicidal ideation, suicidality, and serious suicide attempts were 43%, 44%, and 55%, respectively (Statham et al. 1998). On the other hand, Glowinski et al. included in the study 3,416 Missouri female adolescent twins, finding a concordance rate for suicide attempts of 25% in MZ twins versus 12.8% in DZ twins. The unadjusted odds ratio (OR) for co-twin attempts was higher in MZ twins (11.6) compared to DZ twins (4.2), but after adjusting for psychiatric comorbidity and abuse history, the adjusted ORs were more similar (5.6 vs. 4.0). The heritability of suicide attempts was estimated at 38% (Glowinski et al. 2001). Finally, Fu et al. examined 3,372 male twin pairs in the Vietnam Era Twin Registry (VET) showing that MZ twins more likely to be concordant for suicide attempts than DZ twins, even after adjusting for other risk factors (adjusted ORs 12.06 vs. 7.41). In fact, the unadjusted heritability for suicidal ideation and attempts was 43% and 30%, respectively while after adjustment for psychiatric disorder, combat history, and sociodemographic variables, the heritability estimates were 36.0% for suicidal ideation and 17.4% for attempts (Fu et al. 2002).

Family studies

Family studies compared the rate of suicide or suicidal behaviors in the relatives of individuals with suicidality to those without. Despite variations in outcomes, proband selection, comparison groups, and assessment methods, studies consistently showed that suicidal behaviors clusters within families. It has been indicated that both suicide attempts and completions are part of the clinical phenotype being transmitted, as families of attempters showed higher rates of completed suicide, and families of completers showed higher rates of attempts. However, studies that adjusted for the familial transmission of psychiatric disorders and other risk factors still found a persistent familial effect for suicidal behaviors. These findings suggest that familial aggregation of suicidal behaviors could be due to a unique, genetically transmitted diathesis distinct from psychiatric disorders, transmission of severe or comorbid conditions, imitation, or shared environmental factors (Dinwiddie et al. 2000, Nelson et al. 2000). Powell et al. observed that a family history of suicide was 4.6 times more prevalent in psychiatric inpatients who committed suicide compared to those who did not, even after adjusting for other significant risk factors such as suicidal plans, recent attempts, bereavement, delusions, and chronic conditions (Powell et al. 2000). Furthermore, studies of suicide probands with a familial outcome of attempts or completions have been performed, such as a family study of 58 adolescent suicide victims and 55 community controls, directly interviewing an average of four first-degree relatives per proband. It showed a higher rates of attempted and completed suicide in the relatives of the completers than in the controls (Brent et al.1996); in addition, there was a two-fold excess of suicidal ideation among the first-degree relatives of completers compared to controls, but this difference was not significant after controlling for psychopathology rates. This indicates that while the familial transmission of suicidal ideation is linked to psychiatric disorders, the core liability to act upon

suicidal ideation is the key component of suicidal behaviors that is transmitted within families. Others family studies of suicide attempting probands showed that comparing relatives of 62 adolescent suicide attempters with 70 never-suicidal psychiatric controls, the rate of suicide attempts and completions was higher in the relatives of attempters (16.8%) than in those of controls (7.9%); this difference persisted even after adjusting for psychiatric disorders. Additionally, adolescent attempters with higher impulsive aggression had greater family loading for suicidal behaviors (23.1% vs. 9.9%) (Brent & Mann 2005).

CONCLUSIONS

Although many studies have been produced to delineate the genetic influence of suicide and suicidal behaviors, there still remains a need to validate the initial findings and begin to build a broader framework for understanding this complex phenomenon. It has been proposed that the identification of intermediate phenotypes that may make it possible to establish links between genes and suicide behaviors (endophenotypes) such as personality traits, psychological-cognitive characteristichs, neurochemistry and neuroimaging (Treviño et al. 2011) could represent a promising strategy to overcome the methodological difficulties encountered studying these heterogeneous behaviours.

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Giada Juli: conceptualization, data curation, formal analysis, investigation, methodology, project administration, visualization, validation, writing original draft, writing review & editing, supervision.

Rebecca Juli, Alfredo Juli & Luigi Juli: conceptualization, visualization, literature searches and analyses, review & editing.

References

1. *Asberg M, Traskman L, Thoren P: 5-HIAA in the cerebrospinal fluid: a biochemical suicide predictor? Arch Gen Psychiatry 1979; 33:1193-119*
2. *Austin MC, Janosky JE, Murphy HA: Increased corticotropin-releasing hormone immunoreactivity in monoamine-containing pontine nuclei of depressed suicide men. Mol Psychiatry 2003; 8:324-332*
3. *Bach-Mizrachi H, Underwood MD, Kassir SA, Bakalian MJ, Sibille E, Tamir H, Mann JJ, Arango V: Neuronal tryptophan hydroxylase mRNA expression in the human dorsal and median raphe nuclei: major depression and suicide. Neuropsychopharmacology 2006; 31:814-24*
4. *Bondy B, Buettner A, Zill P: Genetics of suicide. Mol Psychiatry 2006; 11:336–351*
5. *Brent DA, Bridge J, Johnson BA, Connolly J: Suicidal behavior runs in families: A controlled family study of adolescent suicide victims. Arch Gen Psychiatry 1996; 53:1145-1152*
6. *Brent D and Mann JJ: Family Genetic Studies, Suicide, and Suicidal Behavior. American Journal of Medical Genetics Part C (Semin. Med. Genet.) 2005; 133C:13-24*
7. *Coryell W and Schlesser M: The dexamethasone suppression test and suicide prediction. Am J Psychiatry 20011; 58:748–753*
8. *Costanza A, D'Orta I, Perroud N, Burkhardt S, Malafosse, Mangin P & La Harpe R: Neurobiology of suicide: do biomarkers exist? Int J Legal Med 2014; 128: 73-82*
9. *Dinwiddie S, Heath AC, Dunne MP, Bucholz KK, Madden PAF, Slutske WS, Bierut L, Statham DB, Martin NG: Early sexual abuse and lifetime psychopathology: A co-twin-control study. Psychol Med 2000; 30:41–52*
10. *Ernst C, Mechawar N, Turecki G: Suicide neurobiology. Prog Neurobiol 2009a; 89:315–333*
11. *Ernst C, Deleva V, Deng X, Sequeira A, Pomarenski A, Klempan T, Ernst N, Quirion R, Gratton A, Szyf M, Turecki G: Alternative splicing, methylation state, and expression profile of tropomyosin-related kinase B in the frontal cortex of suicide completers. Arch Gen Psychiatry 2009b; 66:22-32*
12. *Fiori LM & Turecki G: Gene expression profiling of suicide completers. Eur Psychiatry 2010; 25:287–290*
13. *Fu Q, Heath AC, Bucholz KK, Nelson EC, Glowinski AL, Goldberg J, Lyons MJ, Tsuang MT, Jacob T, True MR, Eisen SA: A twin study of genetic and environmental influences on suicidality in men. Psychol Med 2002; 32:11–24*
14. *Gabilondo AM, Meana JJ, Garcia-Sevilla JA: Increased density of mu-opioid receptors in the postmortem brain of suicide victims. Brain Res 1995; 682:245-250*
15. *Glowinski A, Bucholz KK, Nelson EC, Fu Q, Madden P, Reich W, Heath AC: Suicide attempts in an adolescent female twin sample. J Am Acad Child Adolesc Psychiatry 2001; 40:1300–1307*
16. *Gross-Isseroff R, Dillon KA, Israeli M, Biegon A: Regionally selective increases in mu opioid receptor density in the brains of suicide victims. Brain Res 1990; 530:312-316*
17. *Karege F, Vaudan G, Schwald M, Perroud N, La Harpe R: Neurotrophin levels in postmortem brains of suicide victims and the effects of antemortem diagnosis and psychotropic drugs. Mol Brain Res 2005; 136:29-37*
18. *Karege F, Perroud N, Burkhardt S, Schwald M, Ballmann E, La Harpe R, Malafosse A: Alteration in kinase activity but not in protein levels of protein kinase B and glycogen synthase kinase-3β in ventral prefrontal cortex of depressed suicide victims. Biol Psychiatry 2007; 61:240-245*
19. *Keller S, Sarchiapone M, Zarrilli F, Videtic A, Ferraro A, Carli V, Sacchetti S, Lembo F, Angiolillo A, Jovanovic N, Pisanti F, Tomaiuolo R, Monticelli A, Balazic J, Roy A, Marusic A, Cocozza S, Fusco A, Bruni CB, Castaldo G, Chiariotti L: Increased BDNF promoter methylation in the Wernicke area of suicide subjects. Arch Gen Psychiatry 2010; 67:258–267*
20. *Kim S, Choi KH, Baykiz AF, Gershenfeld HK: Suicide candidate genes associated with bipolar disorder and schizophrenia: an explanatory gene expression profiling analysis of post-mortem prefrontal cortex. BMC Genom 2007; 8:413-416*

21. *Klempan TA, Rujescu D, Mérette C, Himmelman C, Sequeira A, Canetti L, Fiori LM, Schneider B, Bureau A, Turecki G: Profiling brain expression of the spermidine/spermine N1-acetyltransferase 1 (SAT1) gene in suicide. Am J Med Genet 2009 part B; 150B:934-94*
22. *Mann JJ: Neurobiology of suicidal behavior. Nat Rev Neurosci 2003; 4:819–828*
23. *McGowan PO, Sasaki A, D'Alessio A, Dymov S, Labonté B, Szyf M, Turecki G, Meaney MJ: Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat Neurosci 2009; 12:342–348*
24. *Merali Z, Kent P, Du L, Hrdina P, Palkovits M, Faludi G, Poulter MO, Bédard T, Anisman H: Corticotropin-releasing hormone, arginine vasopressin, gastrin-releasing peptide, and neuromedin B alterations in stress-relevant brain regions of suicides and control subjects. Biol Psychiatry 2006; 59:594-602*
25. *Nelson EC, Grant JD, Bucholz KK, Glowinski A, Madden PAF, Reich W, Heath AC: Social phobia in a population-based female adolescent twin sample: Co-morbidity and associated suicide-related symptoms. Psychol Med 2000; 30:797–804*
26. *Nemeroff CB, Owens MJ, Bissette G, Andorn AC, Stanley M: Reduced corticotrophin releasing factor binding sites in the frontal cortex of suicide victims. Arch Gen Psychiatry 1988; 45:577-579*
27. *Noga JT, Hyde TM, Herman MM, Spurney CF, Bigelow LB, Weinberger DR, Kleinman JE: Glutamate receptors in the postmortem striatum of schizophrenic, suicide and control brains. Synapse 1997; 27:168-176*
28. *Oquendo MA, Russo SA, Underwood MD, Kassir SA, Ellis SP, Mann JJ, Arango V: Higher postmortem prefrontal 5-HT2A receptor binding correlates with lifetime aggression in suicide. Biol Psychiatry 2006; 59:235-243*
29. *Pandey GN, Ren X, Rizavi HS, Conley RR, Roberts RC, Dwivedi Y: Brain-derived neurotrophic factor and tyrosine kinase B receptor signaling in postmortem brain of teenage suicide victims. Int J Neuropsychopharmacol 2008; 11:1047-1061*
30. *Perroud N, Neidhart E, Petit B, Vessaz M, Laforge T, Relecom C, La Harpe R, Malafosse A, Guipponi M: Simultaneous analysis of serotonin transporter, tryptophan hydroxylase 1 and 2 gene expression in the ventral prefrontal cortex of suicide victims. Am J Med Genet Part B 2010; 153B:909–918*
31. *Powell J, Geddes J, Deeks J, Goldacre M, Hawton K: Suicide in psychiatric hospital in-patients: Risk factors and their predictive powers. Br J Psychiatry 2000; 176:266–272*
32. *Punzi G, Ursini G, Chen Q, Radulescu E, Tao R, Huuki LA et al.: Genetics and Brain Transcriptomics of Completed Suicide. Am J Psychiatry 2022; 179:226-241*
33. *Roy A, Segal NL, Sarchiapone M: Attempted suicide among living co-twins of twin suicide victims. Am J Psychiatry 1995; 152:1075–1076*
34. *Roy A, Segal NL.: Suicidal behavior in twins: A replication. J Affect Disord 2001; 66:71–74*
35. *Schulsinger F, Kety SS, Rosenthal D,Wender PH: A family study of suicide. In: Schou M, Stromgren E, editors. Origin, preven-tion and treatment of affective disorders. London: Academic Press, 1979; pp 277–287*
36. *Sequeira A, Gwadry FG, ffrench-Mullen J, Canetti L, Gingras Y, Casero Jr RA, Rouleau G, Benkelfat C, Turecki G: Implication of SSAT by gene expression and genetic variation in suicide and major depression. Arch Gen Psychiatry 2006; 63:35-48*
37. *Statham DJ, Heath AC, Madden PAF, Bucholz KK, Bierut L, Dinwiddie SH, Slutske WS, Dunne MP, Martin NG: Suicidal behaviour: An epidemiological and genetic study. Psychol Med 1998; 28:839–855*
38. *Treviño LJ, Blasco-Fontecilla H., Braquehais MD, Ceverino-Dominguez A, Baca-Garcia E. Endophenotypes and suicide behaviour. Actas Esp Psiquiatr 2011; 39:61-9*
39. *Turecki G, Ernst C, Jollant F, Labonté B, Mechawar N: The neurodevelopmental origins of suicidal behavior. Trends Neurosci 2012; 35:14–23*
40. *Valdizán EM, Díez-Alarcia R, González-Maeso J, Pilar-Cuéllar F, García-Sevilla JA, Meana JJ, Pazos A: α2-adrenoceptor functionality in postmortem frontal cortex of depressed suicide victims. Biol Psychiatry 2010; 68:869-872*
41. *Wender PH, Kety SS, Rosenthal D, Schulsinger F, Ortmann J, Lunde I: Psychiatric disorders in the biological and adoptive families of adopted individuals with affective disorders. Arch Gen Psychiatry 1986; 43:923–929*
42. *Zhang L, Su TP, Choi K, Maree W, Li CT, Chung MY, Chen YS, Bai YM, Chou YH, Barker JL, Barrett JE, Li XX, Li H, Benedek DM, Ursano R: P11 (S100A10) as a potential biomarker of psychiatric patients at risk of suicide. J Psychiatr Res 2011; 45:435–441*

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