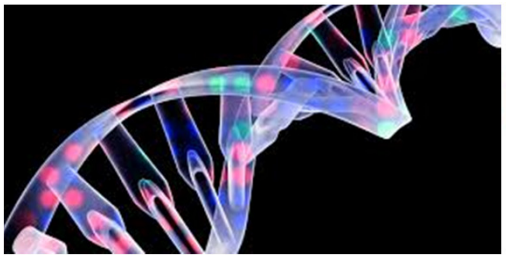
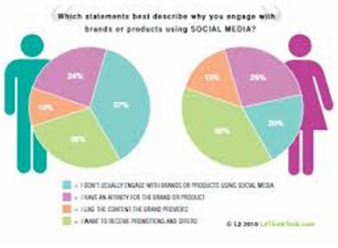
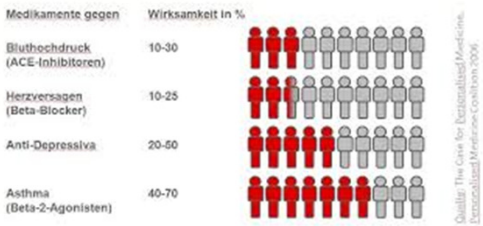
Universität Zürich[UZH]

Soziologisches Institut

Soziologische Forschung mit Biodatenbanken



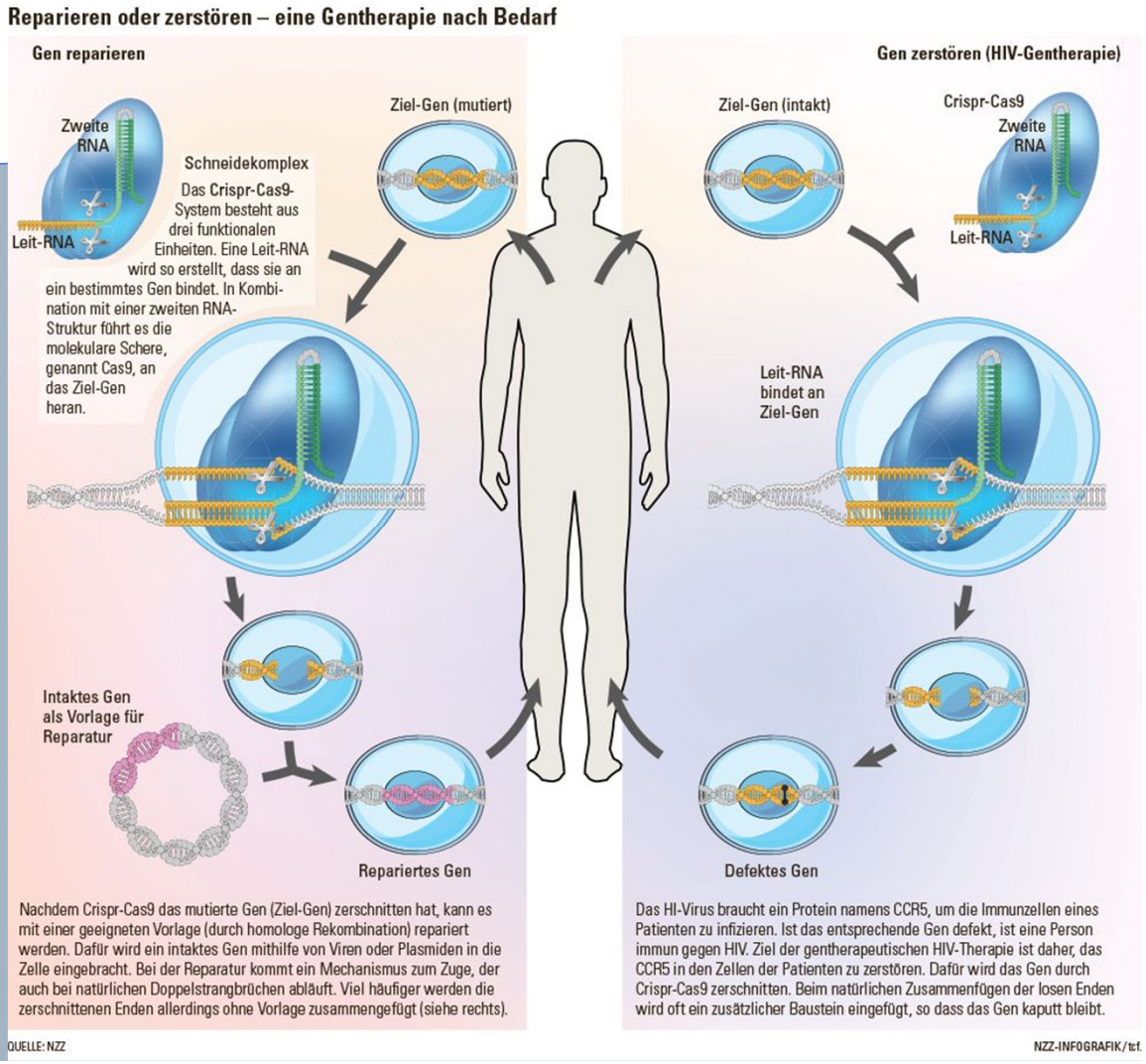




Universität Zürich[UZH]

Soziologisches Institut

Crispr-Cas9



Literatur

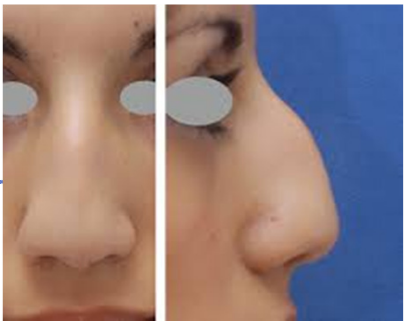
- Eckhardt, A. Navarini, A.A., Recher, A. Rippe, K.P., Rütsche, B., Telser, H., Marti, M. (2014), Personalisierte Medizin, vdf Hochschulverlag AG an der ETH Zürich, TA-SWISS 61/2014.
- Hatemi, P. K., Dawes, C. T., Frost-Keller, A., Settle, J. E., & Verhulst, B. 2011. Integrating Social Science and Genetics: News from the Political Front. Biodemography and Social Biology, 57(1): 67-87.
- Robinson, G.E., C.M. Grozinger, C.W. Whitfield. 2005. Sociogenomics: Social Life in Molecular Terms. Nature Reviews Genetics 6(4) 257-U216.

Inhalt

1. **Biomedizin, personalisierte Medizin, Epigenetik und Biodatenbanken**
2. Sociogenomics – Soziales Leben aus molekularer Betrachtung
3. Integration von Sozialwissenschaften und Genetik

Biomedizinische Entwicklungen

- Personalisierte Medizin erhebt Patientendaten auf der molekularen Ebene (Biomarker) und werte diese informationstechnisch aus um wissenschaftlich fundierte, evidenzbasierte Behandlungsoptionen unter Berücksichtigung der spezifisch die individuellen Merkmale zu finden
- Basis bilden Messdaten zu verschiedenen Ebenen (omics), auf denen der Körper organisiert ist: Genomik (Bauplan eines Organismus), Transkriptomik (Bauanleitung), Proteomik (zusammengebaute zelluläre Maschinerie), Metabolomik (aktuelles Geschehen des Stoffwechsels)
- Instrument der Personalisierten Medizin sind genetische Untersuchungen (Biomarker) und nicht-molekularen Biomarker wie Body-Mass-Index
- Self-Tracking-Sensoren erfassen Daten zu Körperfunktionen und werden mit Biomarkern und Patientenbefragungen kombiniert

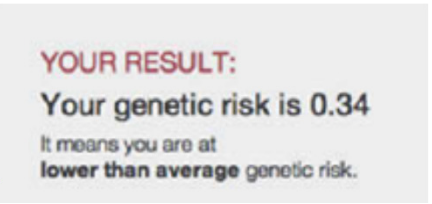


Aktuelle Entwicklungen

- Wandel des Selbstverständnis der Medizin: nicht einzelne Krankheiten, sondern charakteristische Muster von biologischen Eigenschaften eines Menschen stehen im Vordergrund. Die Grenzen zwischen Gesundheit und Krankheit verlieren für medizinische Behandlungen an Bedeutung.
- Schutz von Persönlichkeitsrechten: Personen mit ungünstigen Biomarkern könnten sich im Arbeits- oder Versicherungsbereich Diskriminierungen ausgesetzt sehen.
- Solidarität: Gesundheit und Krankheit rücken stärker in den Verantwortungsbereich der betroffenen Personen -> Aushöhlung des Solidaritätsprinzips?
- Stratifizierung führt dazu, dass Personen in Bezug auf unterschiedliche Chancen einer wirksamen Behandlung unterschieden werden -> Gerecht?
- Entwicklung von Informationstechnologien: elektronisches Patentiendosier, Big Data/Data Mining, Soziale Netzwerke/Medien

Stand der Biomedizin

- Identifikation von Biomarkern zur Vorhersage/Diagnose/Präventation von Krankheiten
- Patienten werden Gruppen zugeordnet, zu denen Forschungsergebnisse existieren (Stratifizierung)
- konventionelle genetische Untersuchungen zu bestimmten Genen sind seit Jahrzehnten etabliert; selektive Analyse einer kurzen Desoxyribonukleinsäure(DNS)-Sequenz geben aber nur die gesuchten Informationen wieder

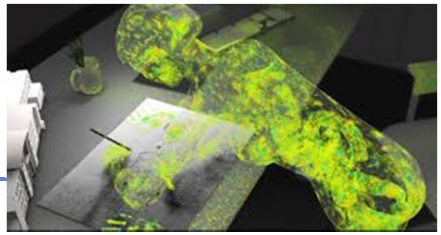


Entwicklungstendenzen der Biomedizin (1)

- Genome Wide Association Studies fokussieren auf variablen Stellen des Genoms. Die DNS von Erkrankten und Kontrollen werden auf krankheitsassoziierte Stellen hin verglichen (mit Replikationskohorte) – die genauen Mechanismen der Krankheitsentstehung müssen mit anderen Studien aufgeklärt werden.
- Next Generation Sequencing (NGS) untersucht die gesamte DNS-Sequenz (Whole Genome Sequencing). Mit dieser Technik können genetische Varianten identifiziert werden, die in der Bevölkerung nur selten vorkommen oder sogar einzigartig sind.

Entwicklungstendenzen der Biomedizin (2)

- Epigenetik befasst sich mit Eigenschaften, die zwar vererbt werden können, aber nicht in der eigentlichen DNS-Sequenz festgelegt sind. Geht auf die Methylierung der DNS zurück, d.h. Bestückung mit zusätzlichen chemischen Gruppen. Hierdurch werden aktive und inaktive Bereichen der DNS markiert. Umweltfaktoren beeinflussen die Epigenetik.
  - Fitnesstraining beeinflusst den Methylierungsstatus mehrerer Gene positiv und ist deswegen mit Diabetes assoziiert.
  - Personen, die vor der Geburt einer Hungersnot ausgesetzt waren, haben noch 60 Jahre später eine veränderte Methylierung.
  - Rauchen der Grosseltern im jungen Lebensalter begünstige noch bei den Enkeln die Entstehung von Asthma.
  - Traumata aus der Verdingung von Kindern in der Schweiz sind erblich auf deren Kinder übertragbar.
- Epigenetische Veränderungen können also dauerhaft verbleiben und biologische Prozesse beeinflussen.



Entwicklungstendenzen der Biomedizin (3)

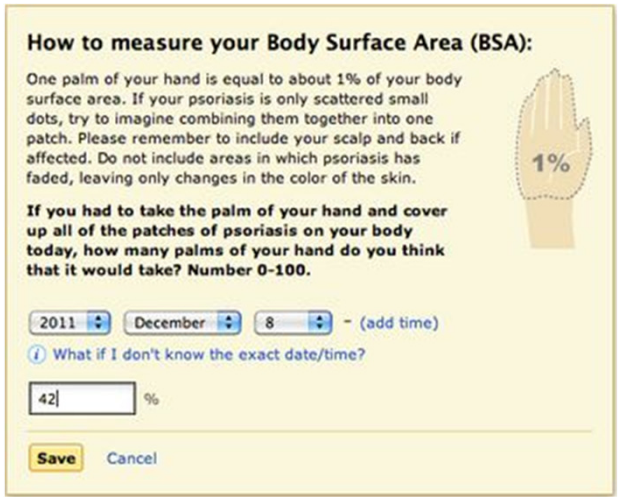
- Transkriptomik ist die genomweite Untersuchung der RNS (Ribonukleinsäure - Bauanleitung der Proteine)
- Proteomik untersucht das gesamte Spektrums der Proteine, die mit einem Gesundheitszustand assoziiert sind. Proteine sind sehr dynamisch, es können grosse Veränderungen innert Sekunden auftreten.
- Metabolomik interessiert für die chemischen Fingerabdrücke, die von zellulären Prozessen zurückgelassen werden, d.h. sie befasst sich mit dem aktuellen Geschehen in de Zelle.
- Mikrobiomik untersucht Bakterienpopulationen in verschiedenen Organen.

Entwicklungstendenzen der Biomedizin (4)

- Pränatale DNS-Analyse untersucht die DNS-Sequenzierung eines ungeborenen Kindes (z.B. über Blut der Mutter), was Rückschlüsse auf Hunderte von Erbkrankheiten und Chromosomenanomalien wie Down Syndrom erlaubt.
- Deep Sequencing erlaubt Tumorzellen früh im Blut zu entdecken.
- Klinische Daten für Medical Data Mining sammeln quantitativ alle Daten der Patienten und können sogar von automatischen Entscheidungs-Unterstützungsalgorithmen benutzt werden.
- Adherence-Tracking verzeichnet per Sensor ob und wann Medikamente eingenommen wurden.

Entwicklungstendenzen der Biomedizin (5)

– Standardisierte Lebensqualitätsmessungen messen den inneren Leidensdruck von Patienten, z.B. mittels Surrogat(bio)markern beim Dermatology Life Quality Index(DLQI)-Fragebogen, mit dem die Lebensqualität bei dermatologischen Erkrankungen erfasst wird.



Big Data und Data Mining

- Biomedizin/Personalisierte Medizin bringen grosse und vielfältige Datensätze (Big Data) hervor, zum Beispiel aus Gentests, Untersuchungen mit bildgebenden Verfahren oder beim Self-Tracking, welche mittels Data Mining ausgewertet werden.
- Es besteht die Vermutung, dass sich in den grossen Datenmengen bisher unbekannte Muster und Zusammenhänge verbergen, die genutzt werden können, um die Gesundheit von Menschen zu verbessern (Vorsicht ist allerdings gegenüber Scheinkorrelationen geboten.)

Biodatenbanken

- Geordnete Sammlungen von Substanzen des menschlichen Körpers, zum Beispiel von Zelllinien oder Blut. Diese Substanzen werden gemeinsam mit Daten über Krankheiten und aus dem Lebensumfeld der Personen, von denen die Substanzen stammen, erhoben und gespeichert.
- Z.B. Die UK Biobank besteht aus 500 000 Personen. Diese Personen gaben Auskünfte über sich selbst ab, stellten biologische Proben zur Verfügung und willigten in eine Überwachung ihres Gesundheitszustands ein.
- International existieren verschiedene breit angelegte Initiativen, um umfassende Biobanken aufzubauen und zu nutzen. In der Schweiz wurden bislang alle Initiativen vom Bundesrat abgelehnt.

Kommerzielles Data Mining

- Um die Potenziale von Big Data und Data Mining im Gesundheitswesen zu nutzen sind Google, Apple und Facebook Vorbild.
- Data Mining kann aus einer Vielzahl einzelner, scheinbar irrelevanter Daten ein detailliertes Bild der betreffenden Person konstruiert werden.
- Self-Tracking dient vordergründig dem persönlichen Data Mining für ein zufriedeneres Leben. Ob und wie die erhobenen Daten im Hintergrund noch anderwärtig ausgewertet werden ist nicht klar. Durch Verbindung der Daten aus verschiedenen Bereichen lassen sich differenzierte Bilder von einer Person gewinnen.
- Beispielsweise erhebt Google bereits Daten aus den verschiedenen Diensten. Diese Daten können mit Gentest-Daten aus dem von Google finanzierten Unternehmen 23andMe verbunden werden.

Austausch von Gesundheitsdaten in Sozialen Medien

- Self-Tracking bedeutet, regelmässig Daten zur eigenen Person zu erheben, aufzuzeichnen und auszuwerten. Dabei handelt es sich um biomedizinische Daten, Verhalten, psychisches Befinden und soziale Aspekte. Kostengünstige Sensoren helfen bei der Erhebung der Daten.
- Soziale Netzwerke sorgen für «patienteninspirierte» oder «patientenbetriebene» Forschung («open source»- oder «crowd sourced»-Forschung)
- *23andMe* bietet Genomanalysen an. Kunden senden eine Speichelprobe ein. Zudem werden die Kunden nach Informationen zum Lebensstil, Medikamentenkonsum, in der Familie vorkommenden Krankheiten und weiteren Informationen gefragt. Ziel ist es, auf diese Weise neue genetische Marker für phänotypische Merkmale, insbesondere Krankheiten, zu finden.

Fazit

- Fortschritte in der Biomedizin und Informationstechnik erlauben kostengünstige Big Data Sammlungen von Gesundheits- und Lifestyledaten von Personen. Diese Daten werden mit anderen Daten verknüpft.
- Fortschritte in der Epigentik legen das Augenmerk auf die Interaktion zwischen Gen und Umwelt. Hierdurch erlangen Sozialwissenschaften an Relevanz für die Biologie und Medizin.
- Die Verfügbarkeit von Daten führt zu Forschung, kommerziellen Anwendungen und institutionellen Veränderungen wie Normen, Werte, Politik etc.

Inhalt

1. Biomedizin, personalisierte Medizin, Epigenetik und Biodatenbanken
2. **Sociogenomics – Soziales Leben aus molekularer Betrachtung**
3. Integration von Sozialwissenschaften und Genetik

Sociogenomics

The goal of sociogenomics is to achieve a comprehensive understanding of social life in molecular terms: how it evolved, how it is governed, how it influences all aspects of genome structure, activity and organismal function.

1. Social life has a biological basis and is therefore influenced to some extent by genes and the forces of evolution.
2. The molecular functions of many genes are highly across species, even for complex trais.

The most progress has been made in the identification of genes that influence animal social behavior.

The link between behavior and genes

- Life in society is often highly structured, with nearly all activities influenced by interactions with other society members. Social animals accomplish activities cooperatively by communication or forms of social organization like dominance hierarchies and division of labor.
- Social regulation influences when, how often, how intensely and with whom activities are carried out.
- Social regulation is understood to involve changes in gene expression in the brain in response to specific social stimuli, which in turn affect behavior.

Measuring the link between behavior and genes

- TRANSCRIPTOMICS measures changes in the expression of genes that correlate with changes in behavior.
- Gene expression is measured in the brains of individuals that have different behaviors. Differences in transcript abundance reflect a mechanistic link between gene and behavior.
- However, some differences in gene expression are a consequence, not a cause, of a behavioral change.

Examples of social behavior studied from a molecular perspective

1. Foraging
2. Mate recognition and courtship
3. Post-mating behavior
4. Social hierarchies
5. Dominance interactions

Emerging Themes

1. Genes involved in solitary behavior are also used for social behavior, indicating that molecular insights from simple behavior can be used to generate candidate genes for more highly derived patterns of social behavior.
2. The genome is highly sensitive to social influence — the social regulation of gene expression is a potent influence on behavior.

Foraging: solitary to social with the same genes

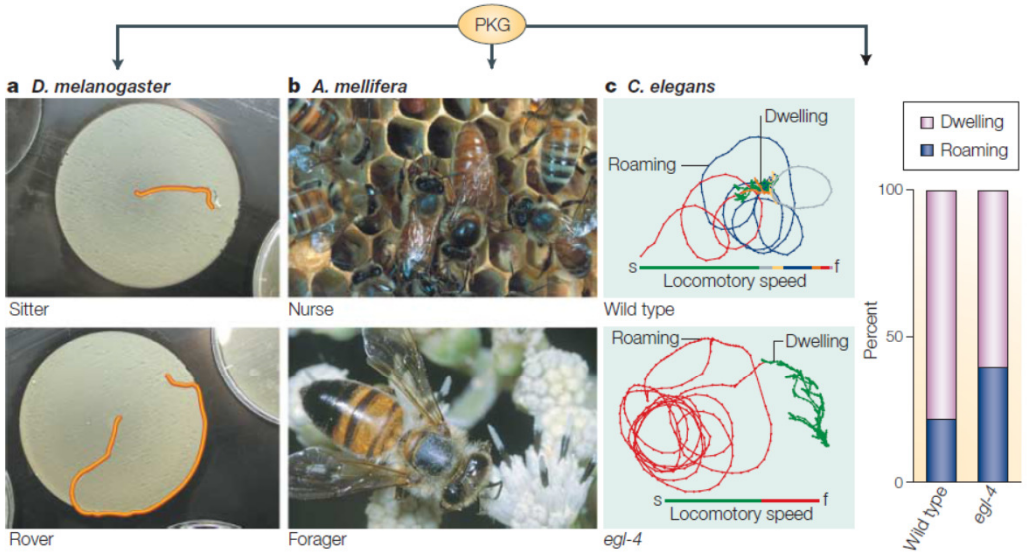


Figure 2 | **cGMP signalling pathways show strong conservation in the regulation of feeding-related behaviours.** Variation in the cyclic GMP pathway is associated with variation in the feeding-related behaviour of *Drosophila melanogaster* 'sitters' and 'rovers'[8] (larvae are shown in **a**); honeybee (*Apis mellifera*) 'nurses' and 'foragers'[10] (**b**); and *Caenorhabditis elegans egl-4* (*egg-laying defective 4*) mutant 'dwellers' and wild-type 'roamers'[15] (**c**). *egl-4* mutants spend more time in the higher-speed roaming state relative to wild-type mutants; this difference is quantified in the histogram to the right of the locomotor tracings. For *D. melanogaster* and *C. elegans*, the variation is genotypic, involving different alleles. For *A. mellifera* it is developmental, involving age-related changes in gene expression in the brain. f, fast; PKG, cGMP-dependent protein kinase; s, slow. Parts **a** and **b** are modified, with permission, from *Nature* REF. 24 © (2002) Macmillan Magazines Ltd. Part **c** is modified, with permission, from REF. 15 © (2002) Elsevier Science.

Example Altruism

Box 4 | **Social microbes**

Managing a social life is complicated — a consideration that has been incorporated into one prominent theory of human brain evolution[108]. But the core elements of sociality — altruism and division of labour — are possible without a brain at all, as seen in some species of microorganisms. Social microbes, with their short generation times and tractability in the laboratory, are proving especially useful for identifying genes that are implicated in social evolution, as indicated below.

Contact site (*csA*)

This gene encodes a homophilic cell-adhesion molecule and, as predicted by Haig[109], seems to function like a green beard gene. When food is scarce, the slime mould *Dictyostelium discoideum* shows reproductive division of labour: free-living individual cells aggregate into a slug, with reproductive spore cells positioned on top of non-reproductive (altruistic) stalk cells[110]. Wild-type cells are more likely to form stalk cells (that is, are more altruistic) than *csA*-knockout cells, and also preferentially allow wild-type, rather than *csA*-knockout, cells to form spore cells[111].

***dif* insensitive mutant (*dimA*)**

The transcription factor that is encoded by this gene illustrates that pleiotropy can promote altruism. *dimA* is required by *D. discoideum* to receive the DIF1 extracellular signal that causes cells to enter the pre-stalk (non-reproductive) stage. *dimA*-knockout cells ignore the DIF1 signal, evading the altruistic fate of stalk formation. They should presumably have a reproductive advantage over wild-type cells. However, in the presence of wild-type cells, *dimA*-knockout cells are excluded from the spore group, so negating any advantage they might gain by evading the stalk fate. Cheating by *dimA* loss of function is prevented because both altruism and reproduction require *dimA* function[112].

Group A signal (*asg*B)

The DNA binding protein that is encoded by *asgB* is involved in growth and development in the bacterium *Myxococcus xanthus*, which forms multicellular aggregations such as slime moulds in response to starvation. Strains that have a mutation in this gene 'cheat' and produce a higher proportion of spore cells relative to their representation in an aggregating population[113]. The maintenance of reproductive division of labour in *M. xanthus* indicates that cheating is kept in check by the effects of other to-be-discovered genes, as in *D. discoideum*. Alternatively, the persistence of cheaters could reflect the balance of population dynamic forces[114].

Parental care: epigenetic regulation

- Rat mothers differ strikingly in how they care for their offspring. Those that lick, groom and nurse their pups extensively endow them with two important attributes: better tolerance of stress and good mothering skills when they themselves get old enough to reproduce. This is because frequent contact of this type increases the expression of the genethat encodes a glucocortocoid receptor in the hippocampus, and greater hippocampal density of these receptors enables the animals to better regulate their response to stress hormones.
- A similar GENOTYPE X ENVIRONMENT INTERACTION has been reported for ‘resilience’ in humans.

Genes that are responsive to social status (1)

- Dominant males are aggressively territorial, brightly coloured, have high levels of circulating testosterone and enjoy high levels of reproductive success. Subordinate males lack all these attributes and their derived reproductive advantages.
- Dominant males have larger hypothalamic neurons that contain the neuropeptide gonadotropinreleasing hormone (GnRH) than subordinate males.
- Non-territorial males that move up in social rank and acquire a territory rapidly show an increase in GnRH gene expression and acquire the suite of characteristics that is associated with dominance.

Genes that are responsive to social status (2)

- Dominance-related interactions often begin with threatening behavior and often this posturing is sufficient to decide the outcome and produce a winner and loser.
- In the dominance hierarchies winners are more likely to dominate in future encounters, whereas losers are more likely to retreat.
- The effects of previous social experience is mediated by social regulation of two serotonin-receptor subtypes, 5HT1 and 5HT2.

Future prospects and challenges

- Many social behavior are sensitive to context and must be studied under natural conditions. This means that behavioral analysis must be approached in both the field and the laboratory. An eclectic mix of species is required to capture the broad range of phenomena that is encompassed by sociality.
- A truly rigorous molecular analysis of sociality requires the ability to establish causal relationships between the effects of genes on social behaviour, and vica versa. Idea to test it via new therapeutics that affect the genome…

Inhalt

1. Biomedizin, personalisierte Medizin, Epigenetik und Biodatenbanken
2. Sociogenomics – Soziales Leben aus molekularer Betrachtung
3. **Integration von Sozialwissenschaften und Genetik**

Traditional social science and behavioral genetic

- Traditional social science models assumes that human behavior and social attitudes are almost entirely the product of environmental influences. Even though it is common to use biological indicators such as gender as predictors, the effects are interpreted as environmental or socialized. The assumption is that all people start with the same inherent disposition.
- Behavioral genetic analyses assume that dependent and independent variables may be a function of both genes and environment. The focus is on understanding the sources of individual variability and the inherent assumption that people have different dispositions.
- Rather than treating “social” and “genetic” theories as competing models, the goal is to treat them as complementary approaches.

Twin and Kinship Models: Partitioning Genetic and Environmental Variance (1)

- Comparing the co-twin correlations for a given trait between a population of twin pairs who are genetically identical but have the same familial environment to the co-twin correlations of a population of non-identical twin pairs who share on average 50 per cent of their differentiating DNA and who also have the same family environment allows researchers to partition what part of the variance in a given trait is accounted for by genetic and environmental factors.
- The general liberalism-conservatism dimensions and most individual attitudes were accounted for by a function of genetic inheritance (0.2 and 0.6) and unique environmental influence (0.4 and 0.8). Only for party identification, no genetic influence was found.

Twin and Kinship Models: Partitioning Genetic and Environmental Variance (2)

- The results have fundamentally altered the ways social scientists approach the study of attitudes.
- For example, the political affiliations and attitudes of parents and offspring and spouses are highly correlated. This concordance has long been assumed to be evidence of familial socialization. The suggestion that ideological or attitudinal transmission might be other than social was rarely, if ever, considered.
- In this way, twin models have provided the necessary empirical venue for testing such assumptions.

Gene-Environment Interactions

- Independent effects of genes and the environment is a first step in explicating the nature of a trait of interest.
- Virtually every socially relevant behavior is a complex function of both genetic and environmental influences. Thus, it is necessary to incorporate a method whereby genetic and environmental factors interact to moderate the behaviors individuals engage in.
- A gene-environment interaction occurs when genetic factors control the sensitivity to the environment. Thus, the influence of an environmental factor on a behavior is conditioned by a person's genotype, or conversely, the genotype's effect is moderated by some environmental exposure.

"Broad heritability-environment interaction" method

Rather than modeling attitudes using the linear equation where the variance (V) of trait (t) is a function of genes (*A2*) and environment (*C2* + *E2*), a GxE twin model expresses the variance associated with each of the three components (ACE) as a linear interaction with the specific environment measured.

$(Vt = (A + \beta a * Event)^2 + (C + \beta c * Event)^2 + (E + \beta e * Event)^2)$.

Genetic effects can be partitioned into a baseline or average influences independent of the environment measured (analogous to an intercept in linear regression), and the marginal effect of the specific environmental event (i.e., slope).

Example

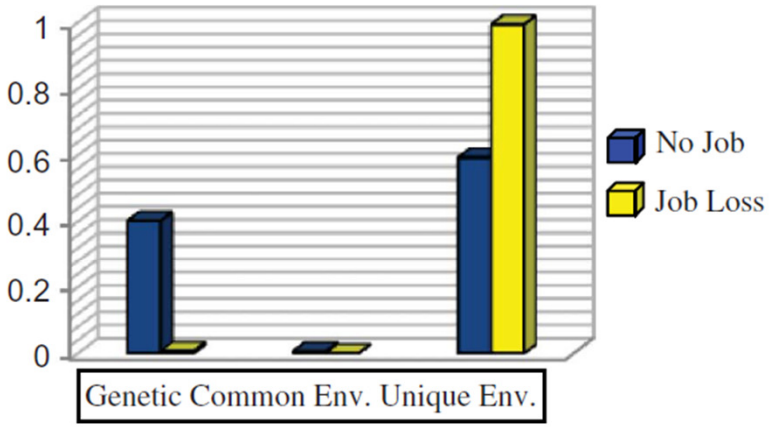


Figure 2. Change in heritability estimates of attitudes on *federal housing* as a function of *losing your job*. (color figure available online)
Note: Figure derived from Hatemi, 2010b.

The complex relationship between gene-environment interaction

- If genes motivate people to seek out certain environments or social situations and those environments influence behavior, the environments measured are no longer entirely exogenous, and it becomes difficult to quantify the genetic effect on a behavior or attitude separately from its environmental effect.
- For example, it as been found that people “select into” getting a divorce, in part based on their genetic disposition. In this way, the event of getting a divorce could not be considered truly exogenous, and any gene-environment interaction with the event of getting divorced would be confounded.

Candidate Gene/Marker Studies

- Identify within a population whether the incidence of a specific version of a gene, most often an allele, is more common than would be expected due to chance among individuals exhibiting a particular trait. Candidate genes are typically selected on the basis of previous associations with behaviors.
- Case-control designs compare the frequency of alleles or genotypes among subjects that exhibit a trait of interest (e.g., voting) to subjects who do not and test the null hypothesis of no association.
- Family-based designs compare whether offspring who exhibit the trait of interest (e.g., vote) receive an allele from their parents more often than would be expected by chance. This method reduces the probability of false-positive signals that may arise from what is known as *population stratification*.

Candidate Gene x Environment Interactions

- Candidate gene by environment interaction studies seek to identify the interactions between *specific* genetic variants and specific environmental stimuli are associated with differences in behaviors. Regression-based techniques are used to test the significance of interaction terms between specific genetic marker and specific environmental stimuli.
- For example, exposure to diverse viewpoints in adolescence, as measured by the number of self-reported friendships, enhances a liberal political identification for those people who carry the DRD4-R7 allele, who may be genetically predisposed to be novelty-seekers. People with the R7 allele are no more likely to have a large number of friends than those without it, but the effect of this exposure has a differential effect on the development of their ideology.

Genome-wide Analyses

- Systematically scan the entire genome for markers significantly related to the traits of interest. In this way, they are not constrained by prior hypotheses.
- Genome-wide linkage require a large sample of related individuals. Genome-wide association rely on a sample of unrelated individuals.
- Due to the simultaneous exploration of hundreds of thousands of markers, a genome-wide association scans GWAS requires large sample sizes and expensive genotyping, and it demands an extremely high threshold for significance: $p < 5\times10-$ or better.
- GWAS studies for traits are now underway and should begin producing results in the near future.

Unique considerations of Candidate Marker and Genome-wide Studies

- Blood or saliva must be collected, and researchers must have training in molecular biology and be cognizant of the additional ethical considerations, subject protections, data safety, and sample collection protocols necessary for dealing with biological specimens, as well as access to proper processing, genotyping, storage facilities and methodological expertise.
- Furthermore, the funding mechanisms in the social sciences for these additional expenses are limited.

Limitations of Candidate Marker and Genome-wide Studies (1)

- What appears to be a significant causal relationship between a genetic variant and a trait of interest may be due to chance. Statistical evidence for an association between an allele and a phenotype comes from one of three situations: (1) The allele itself might be functional and directly affect expression of the trait, (2) the allele might be correlated with another causal allele, (3) the association could be attributable to chance, artifact of the sample, confounding or selection bias (e.g., population stratification).
- So far, very few candidate genetic marker studies have survived long-term replication, and fewer still are validated by genome-wide approaches, which suggest that many significant results may be an artifact of the specific sample being studied rather than a genuine relationship.

Limitations of Candidate Marker and Genome-wide Studies (2)

- Studies that use the exact same genetic markers have been coded in different ways, achieving significance in their respective studies. For example, the Taq1a variant of ANKK1, part of the dopamine pathway, comes in three forms: TT, TC, and CC. Three studies that used the same AddHealth data coded Taq1a in three different ways: (1) as the number of C alleles (0, 1, and 2), as C/C versus the combination of TC and TT, (3) as T/C versus the combination of CC and TT. The lack of a uniform coding scheme makes it difficult to ensure accurate replication and interpretation.
- Candidate gene studies capture only a single polymorphism for a single gene even though it is known that it is unlikely that genes act independently.

Limitations of Candidate Marker and Genome-wide Studies (3)

- Proper interpretation of results is important. For instance, Settle et al. (2010) reported that people with 10 friends who have two copies of the 7R allele of DRD4 would have the effect of increasing ideology in the liberal direction by about 40 per cent versus those who do not have two copies of 7R allele but also have 10 friends. A result of this magnitude due to a single variant on a single dopamine receptor is unlikely. In candidate gene studies, effect sizes are often inflated due to the statistical model. This is of greater concern in small samples.
- Possibly the greatest concern in candidate gene studies are the false-positives reported in candidate gene-environment interaction studies. Studies that find no main effect but find an interaction do not tend to survive long-term replication.