# Machine Learning and Personal Genome Informatics Contribute to Happiness Sciences and Wellbeing Computing

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#### **Abstract**

Two big recent revolutions: machine learning technologies; such as "deep learning" in Artificial Intelligence (AI), and personal genome informatics in biomedical science, provide us with new opportunities for understanding human happiness. Our ongoing important challenges are to discover our own truly meaningful personal happiness with the aid of AI and personal genome technologies. We have been developing a personal genome information agent entitled MyFinder, which supports searching for our inherited talents and maximizes our potential for a meaningful life. In the MyFinder project, we have provided a crowd-sourced DIY (Do it yourself) genomics research platform and conducted various "citizen science" projects in health and wellness. In this paper, we discuss how machine learning technologies and personal genome informatics might contribute to happiness sciences. We introduce the "Social Intelligence Genomics and Empathy-Building Study" and report the preliminary results of applying deep learning and six other machine learning algorithms for predicting social intelligence levels from nine SNPs genetic profiles. We discuss the possibilities and limitations of applying machine learning technologies for personal happiness trait prediction. We also discuss future AI challenges in the context of wellbeing computing.

#### Introduction

The definition of "sense of happiness" varies from person to person. However, if the mechanisms that make people's brains and bodies feel happy and the factors causing individual differences of feeling happiness are identified, different types of a sense of happiness which are hard to distinguish subjectively could be distinguished objectively

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and sensitively. In this paper, we discuss a method of objectively evaluating a subjective sense of happiness based on genetic information suggestive of the relationship with a eudaimonic (pursuing a purpose of life) / hedonic (pursuing pleasure) sense of happiness. We also discuss the relationship between how a sense of happiness changes the impact on genes and bodies, and identify and estimate the behaviors and habits that increase an individual's sense of happiness. To summarize, the purpose of this paper is to analyze the factors affecting a sense of happiness based on information science and to develop a method enabling visualization of these factors. Our challenge is to develop a method, through machine learning, to specify (estimate) the relationship between behaviors and habits that increase a sense of happiness and genetic mutation.

#### **Happiness Sciences**

## Research of "a sense of happiness" by community computing

Killingworth (Killingworth 10) kept track of daily events that made individuals feel a sense of happiness in real time through analyzing many samples, and reported that a sense of happiness highly correlated with "what individuals were thinking" rather than "what individuals were doing"; that individuals felt a highest sense of happiness when they focused on a task at hand; and that a sense of happiness decreased when they could not focus on things. Fowler (Fowler 08) also reported, from analysis that evaluated the relationship between social networks and level of happiness, that happy individuals were more inclined to connect with other happy individuals, and that if a maximum of "acquaintances of acquaintances of the individuals" were happy, the individuals were more in-

clined to feel a sense of happiness; that if, rather than their partners or relatives, their friends who physically lived close to them were happy, they were more inclined to feel a sense of happiness. Compared to this research, we focus on the extraction of the cognitive bias (Kahneman 11, Minskey 06, Takebayashi 14) and individual differences (Perry 08), and aim at estimating / evaluating "a sense of happiness" using personal genome information (Ashley 10, Butte 08, Kido 13b).

#### Estimating a sense of happiness by social genomics

Dr. Steve Cole et al. is currently studying how a way of thinking influences gene expression (Cole 13). It has been pointed out that a solitary person has a higher tendency of becoming sick. Dr. Cole et al. found that people who are isolated from society and people who have a chronically strong sense of isolation had more than a 30% change in the average expression of 209 types of genes (CTRA gene expression) involving the immune system, compared to those who were not (Cole 07).14 people with an average age of 55 were analyzed for gene expression in white blood cells by DNA microarray. They were separated into a sociable group and a lonely group based on a questionnaire regarding a sense of loneliness (Russel 78). Compared to the sociable group, the lonely group had overexpression of 78 genes related to inflammation as well as lowered expression of 131 genes related to antibody production and anti-virus reaction.

In addition, Dr. Cole's research team also studied how a sense of happiness influences immune cells and found that gene expression changes depending on the type of sense of happiness (Cole 13). "Hedonic" (a sense of happiness devoted to pleasure) is a sense of self-satisfaction by fulfilling material desire and immediate urges such as "happiness from eating delicious food" and "happiness from purchasing what you wanted". On the other hand, "eudaemonic" (life pursuing sense of happiness) is a sense of deep happiness through having purpose and meaning in life such as "there is direction and meaning in life" and "I have something that I can contribute to society". 80 healthy people from 35 to 64 years old were asked to answer hedonic or eudemonic questions and the correlation with genes of immune cells in blood were studied. For the hedonic sense of happiness, gene expressions representing a feeling of loneliness were found, while for the eudaemonic sense of happiness the gene expressions related to inflammation were repressed and there was an activation of the gene expressions related to anti-virus reaction (Cole 13). People with a high hedonic sense of happiness do not necessarily feel unwell or unhappy, rather they say that they feel that "my life is fulfilled", suggesting very positive response at the conscious level. However, it is very interesting that there were negative influences at the gene expression level among people with a high hedonic sense of happiness. It will be a major challenge to specify (estimate) behaviors that increase or decrease the gene expression for a eudaemonic and/or hedonic sense of happiness as discussed, through machine learning from "data" of daily life activity or sleep patterns. Using gene expression correlating with the above mentioned sense of happiness as well as a bio-marker molecule like the "oxytocin" hormone, which is closely related to interpersonal relationships and a sense of trust, it may be possible to measure and visualize the conventional sense of happiness as an objective state of the body.

#### Positive computing and big data

Rafael (Rafael 14) et al. proposed a paradigm called Positive Computing, a technology aiming for "Wellbeing and Human Potential". Recently, it has become possible to pursue events where people felt a sense of happiness in real time by using wearable devices through analyzing many samples (Killingworth 10), and to analyze the characteristic of connections among people who felt a sense of happiness through their social network (Fowler 09). If the information analysis of this big data and the gene expression analysis are combined, it may become possible to show as objective data when and in what kind of conditions people a tendency to feel a sense of happiness have. We think that it is now necessary to pioneer a new research field on wellbeing computing, focusing on important issues like "what kind of influence the rapid changes in modern lifestyles have on a person's mind and body".

# MyFinder: Machine Learning and Personal Genome Informatics for knowing our self.

In this research, we accumulate, create, and evaluate various knowledge to promote a sense of happiness using a citizen science approach (cloud sourcing) (Swan 12ab). We have proposed a personal genome information environment "MyFinder" Concept and evaluated a new research framework and basic technologies (Kido 11ab, Kido12, Kido13abc, Kido14ab, Kido15ab). In the MyFinder Concept, we have addressed "scientific discovery by community computing" based on the agenda to understand how a rapid change of life styles today evolutionally affects individuals both psychologically and physically. Our idea is "to monitor daily physical, chemical, and mental stresses and investigate the relationship with genetic mutation by observing and analyzing eating habits, sleep patterns, working styles, time management styles, social interactions, hobbies, and preferences every day by an intelligence agent" (Kido 11b). In order to achieve this purpose, we have evaluated the items with our own genetic data (Kido 13b) and various self-tracking affective data (Picard 00).

Our research is to implement the MyFinder Concept with a theme of "individual's sense of happiness", launch a participatory community via the Internet, and aim at scientific discovery by searching for factors that affect an individual's sense of happiness (e.g. behaviors and habits) and biomarkers (oxytocin, gene group etc.) to objectively evaluate the sense of happiness.

#### **Social Intelligence Genomics Study**

We report new findings of the "Social Intelligence Genomics and Empathy building Study" introduced in (Kido 13, Swan 14). The overall summary of this project is explained at the following website: (http://diygenomics.pbworks.com/w/page/48946791/Social%20Intelligence). We will update this project with further advancing analyses.

#### Objective of the Project

The purpose of this project is to confirm and extend research linking social intelligence and genetic profiles.

#### **Hypothesis**

Individuals with certain genetic polyphenism might exhibit a greater natural capacity for improving "social intelligence".

#### **Study Design**

#### A: Selection of Candidate Genes

A literature review was conducted on mental performance and social intelligence researches, such as optimism and empathy, extraversion and altruism. 9 SNPs shown in Table 1 were selected for analysis.

	CNID	D. C	G .
Gene	SNP	Reference	Comment
OXTR	rs53576	[Saphire11]	Optimism
DRD2	rs12364283	[Pecina12]	
	rs2283265	[Pecina 12]	Openness to expe-
	rs4274224	[Pecina 12]	rience
	rs1076560	[Pecina 12]	
	rs4581480	[Pecina 12]	
DRD2/ANKK1	rs1800497	[Smillie 11]	Extraversion
COMT	rs4680	[Reuter 11]	Altruism
	(Val158Met)		
BDNF	rs6265(Val6	[Madrigal09]	Neuroplasticity
	6Met)	1	1 .

Table 1. Analyzed Single Nucleotide Polymorphisms (SNP).

#### **B:** Phenotype Data

Recognized standard online survey questioners were used for the phenotype assessment of social intelligence; IRI: Interpersonal Reactivity Index (28 questions) EQ test: Empathy Quotient test (Baron-Cohen) (60 questions)

#### C: Implementation of a Citizen Science Project

We have been conducting this study using a crowdsourced cohort entitled Genomera. (http://genomera.com/studies/

social-intelligence-genomics-empathy-building) This study started in April 2012. By December 2015, a total of 68 volunteers (28 males, 20 females, 20 unknown) had participated. 38 volunteers made their age public (from 26 to 66 years old) and the vast majority was living in the Unites States (but a few were not). 24 volunteers disclosed their race and most of them were European. 24 volunteers provided shared genotype data for the 9 SNPs (28 volunteers for the 8 SNPs, removing rs2283265 from 9 SNPs) from the 23andMe report. 24 genotype samples for 9SNPs are available for the EQ phenotype and 20 genotype samples are available for the IRI phenotype.

#### D: Analyses

#### **Genetic Association Analyses**

We tested the statistical associations between genotype profiles and phenotypes (EQ Score and IRI Score). For each of 9 SNPs and 2 phenotypes (EQ Score and IRI Score), the Kruskal-Wallis test was conducted for evaluating the strength of correlations with p-value.

### Phenotype Predictions from Genomic Profiles by Machine Learning Algorithms

We evaluated the prediction abilities of 7 machine learning algorithms: adaboost, deep learning (Hinton 15), bagging, CART, Neural network, Random Forest, and SVM. First we categorized the EQ Score into 3 groups (Low, Middle, and High) using the threshold values in Table 2.

EQ class	Threshold	
Low	EQScore < 39	
Middle	39<=EQScore <46	
High	46<=EQScore	

Table 2. Categorization of EQ Scores

We tried to predict EQ class from the 9 SNPs genotype profiles by applying machine learning algorithms.

We used the R functions (shown in Table 3) with default parameter values for each of the 7 algorithms.

algorithm	R library, function	Comments
adaboost	adabag	Boosting (Weak learner
	adaboost()	is decision tree)
bagging	Ipred	Bagging (Weak learner is
	bagging()	decision tree)
CART	Rpart	Decision Tree
	rpart()	
deep learn-	h2o	Deep learning neural
ing	deep learning()	networks
Neural	nnet	Single hidden neural
Network	nnet()	network
Random	randomForest	Ensemble learning meth-
Forest	randomForest()	od for classification, re-
		gression
SVM	Kernlab	Support vector machine
	ksvm()	

Table 3. R functions for machine learning algorithms

By the Leave-one-out cross-validation method, we compared the accuracy rates of the predictions of 7 machine learning algorithms. The accuracy rates are calculated by "#accurate\_predictions / (#accurate\_predictions + #error\_predictions)". Since we applied the Leave-one-out cross-validation method to the 24 samples of EQ class predictions, we tried 24 test predictions and calculated accuracy rates. (For each test prediction, we picked up 1 sample for the test data and the remaining 23 samples were used as training data.)

#### **Preliminary Results**

#### **Genetic Association Analyses**

Correlation between 9SNPs and two scores of self-reporting tests, EQ and IRI, are shown in Figure 1. SNPs are shown on the x-axis and the negative log of the p-value (-log(p-value)) is shown on the y-axis. Each plotted point corresponds to a single SNP. Blue represents association with the EQ Score and red represents association with the IRI Score. The higher a point is on the vertical axis, the stronger the correlation. The SNP most strongly correlated with the EQ Score (blue points) was rs6265 and the second was rs53576. On the other hand, we could not find strong associations with the IRI Score (red points). (We could not calculate p-value for rs4581480, since it didn't have three clusters of genotypes.)

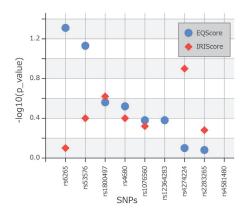


Figure 1. Correlation between Single SNPs and EQ /IRI Scores (p-value distribution)

The relationship between the rs6265 genotype and the EQ score is shown in Figure 2 (A). The x-axis shows rs6265 (a polymorphism of the BDNF gene) and the y-axis shows the EQ Score. People with the CT genotype (n=9) had the lowest EQ Score of 39.6, whereas people with the TT genotype (n=3) had the highest EQ Score of 46.7. The difference in EQ scores between people with the CT geno-

type and people with the CC/TT genotype was statistically significant (p=0.0167).

The relationship between the rs53576 genotype and the EQ score is shown in Figure 2 (B). People with the AA genotype (n=5) had the lowest EQ Score of 38.2, whereas people with the AG genotype (n=14) had the highest EQ Score of 45.1. The difference in EQ scores between people with the AA genotype and people with the AA/AG genotype was statistically significant (p=0.0240).

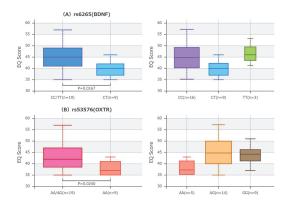


Figure 2. Significant Correlations between EQ Score and the 2 SNPs: (A) rs6265 (BDNF) genotypes, (B) rs53576 (OXTR) genotypes

#### **Predictions by Machine Learning Algorithms**

The comparison of prediction results of EQ class (low, middle, and high) from 9 SNPs with seven different machine learning algorithms is shown in Figure 3.

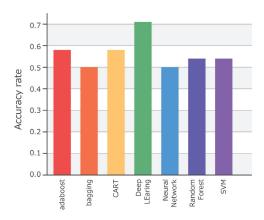


Figure 3. Comparison of accuracy rates of EQ class predictions with 7 machine learning algorithms.

The names of seven machine learning algorithms are shown on the x-axis and the accuracy rates of EQ class predictions are shown on the y-axis. As shown in Figure 3, deep learning outperformed other six machine learning algorithms in this EQ class prediction task. The accuracy rate of the deep learning algorithm was 70.8 percent (17/24), followed by 58.3 percent (14/24) for adaboost and CART.

#### **Discussion**

#### Interpretation of Preliminary Results.

The preliminary results of this study are that two genotype SNPs (BDNF rs6265 and OXTR rs53576) were favorably correlated with test scores for empathy phenotype tests, EQ. This section offers a speculative interpretation of this. The OXTR rs53576 result can be seen as confirmatory of other studies that have previously linked the OXTR rs53576 genotype GG with a propensity for empathy in individuals. The other result with BDNF rs6265 is also to some degree a replication of other study results, but may offer something new in social intelligence and empathic response. BDNF (brain-derived neurotrophic factor) is a nerve growth factor protein that is generally involved with nerve growth in the brain, and pertains to many functions of human development, pathology, and social behavior. Regarding pathologies, BDNF has been linked to illnesses as diverse as schizophrenia, epilepsy, Alzheimer's disease, neuroticism, and depression (Terracciano 10). Beyond pathology, BDNF is associated with neuroplasticity: the brain's ability to rewire itself on the fly to form new synapses (Chaieb 14). One study found that persons with the favorable BDNF genotype (CC) displayed 20% greater neuroplasticity than counterparts (McHughen 10, Madrigal 09). Another study posited that BDNF might be a predictor of general intelligence and cognitive function in everyday decision-making (Rostami 11). Another study found that persons with the favorable BDNF genotype experienced reduced social stress sensitivity (Winkel 14) and that BDNF circulating in the brain might generally promote positive social feelings (Panksepp 12, Goleman 07). Thus, the link found in this study between BDNF and empathic response can be explained in that the greater neuroplasticity available for persons with the favorable BDNF genotype may help to contribute to having more empathy available for the learning and operation of social situations. Also notable with BDNF is that, unlike what might be assumed to be genomic fixity, intervention for BDNF circulation is available as exercise has been found to increase levels three-fold (Szuhany 15, Denham 14).

#### **Future AI Challenges.**

#### Braincloud: Happiness is a Big Data Problem

The topic of this paper is how machine learning and personal genome informatics might contribute to an understanding of happiness sciences and wellbeing. We conclude from this investigation that happiness might be best framed as a 'big data problem.' Significant AI progress has resulted from considering the 'unreasonable effectiveness of mathematics' (Wigner 06) and the 'unreasonable effectiveness of data' (Halevy 09). The key point in making progress was having sufficiently large data corpora over which to run fairly straightforward mathematical and machine learning algorithms. A similar transformation has occurred in health where the bioinformatics and 'omics' era of big health data has allowed biology to also be reconfigured and digitized as AI, math, and information technology problems (Kido 13, Swan 12a). The next stage of 'biology as a math problem' is 'the brain as a math problem,' which would include everything from the underlying biophysiology to user-evaluated affect, emotion, and wellbeing. Happiness can thus be seen as a big data problem in the sense that many different data streams can start to be collected and analyzed towards the pursuit of a general understanding of well-being. This could include a more continuous life-logging operation for all individuals of physiological, neural, and psychological data (canvassed objectively by quantified-self gadgetry and subjectively by user input). These data could be connected in a secure braincloud format where individuals might collect and track their own data as well as share it into pooled cloudminds for research and preventive medicine purposes (Swan 16). In the current study, we connected two dots, a link between favorable genotypes and social intelligence, which could start to contribute to a more global understanding of happiness and well-being.

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#### **Contributions**

The paper was primarily conceived and written by Takashi Kido. Melanie Swan contributed to the discussion section.

#### References

Ashley, E.A., Butte, AJ et al. (2010) "Clinical assessment incorporating a personal genome." Lancet, 375, (9725): pp. 1525-1535

Butte, A.J. "The ultimate model organism." Science, 320 (4), pp.  $325-327 \ (2008)$ 

- L Chaieb, A Antal, GG Ambrus, W Paulus, 2014. Brain-derived neurotrophic factor: its impact upon neuroplasticity and neuroplasticity inducing transcranial brain stimulation protocols, Neurogenetics 15, , 1-11
- S. W. Cole, et. al., (2007) "Social regulation of gene expression in human leaukocytes", Genome Biology, Volume 8, Issue 9,.
- B.L, Fredrickson, K. M. Grewen, S. W. Cole, et. al., "A functional genomic perspective on human well-being", PNAS, vol. 110, no. 33, (2013)
- Denham, J., Marques, F.Z., O'Brien, B.J., Charchar, F.J. 2014. Exercise: putting action into our epigenome. *Sports Medicine* 44 (2):189-209.
- James H Fowler, Nicholas A Christakis, (2009) "Dynamic spread of happiness in a large social network: longitudinal analysis of the Framingham Heart Study social network", BMJ: British medical journal, pp. 23-27
- Goleman, D. 2007. Social Intelligence: The New Science of Human Relationships. New York NY: Bantam.
- Halevy, A., Norvig, P., and Pereira, F. 2009. The Unreasonable Effectiveness of Data. *IEEE Intelligent Systems* 24(2):8-12.
- Yann Le Cun, Yashua Bengio and Geoffrey Hinton, (2015) "Deep Learning", Nature, Vol. 521, pp. 436-444,
- Kahneman, D., Thinking, Fast and Slow. New York, NY: Farrar, Straus, and Giroux. (2011)
- Kido, T., (2011) How do I live? : Searching for ourselves through genome decryption. Hoshinowakai
- Kido, T., (2011) Genetics and artificial intelligence for personal genome service -MyFinder: Intimate community computing for genetic discovery-, AAAI 2011 Spring Symposium
- Kido, T., (2012) Self-Tracking Mindfulness Incorporating a Personal Genome, AAAI 2012 Spring Symposium
- Kido, T., Swan, M., (2013a) Exploring the Mind with the Aid of Personal Genome –Citizen Science Genetics to Promote Positive Well-Being, AAAI 2013 Spring symposium
- Takashi Kido, Minae Kawashima, Seiji Nishino, Melanie Swan, Naoyuki Kamatani, and Atul J Butte, 2013. Systematic evaluation of personal genome services for Japanese individuals, Journal of Human Genetics, Nov, 58(11): pp. 734-41.
- Kido, T., (2013)MyFinder Concept: Self-searching through personal genome. The Journal of the Japanese Society for Artificial Intelligence. Volume 28, Number 6, pp.840-850,
- Takashi Kido, Melanie Swan, 2014. Know thyself: Data driven Self-Awareness for Understanding our Unconsciousness Behaviors, The AAAI (The Association for the Advancement of Artificial Intelligence) 2014 Spring Symposia, Big data becomes personal: From Knowledge into Meaning, pp. 23-28.
- Kido, T., Kamatani, N., (2014)Scientific proof for personal genome medicine, Progress of medicine Current genetic medicine and genome medicine in the near future -. Vol. 250, No. 5, pp. 336-340.
- Takashi Kido, Melanie Swan, (2015) "Ambient Intelligence and Crowdsourced Genetics for Understanding Loass Aversion in Decision Making", The AAAI (The Association for the Advancement of Artificial Intelligence) 2015 Spring Symposia, Ambient Intelligence for Health and Cognitive Enhancement, pp. 19-27,
- Kido, T., Kawashima, M., (2015) "Socio-psychological evaluation on personal genome information: Changes in social consciousness and insights into how to disclose disease risk

- information". The Japan Society of Human Genetics, 60th symposium
- Killingsworth MA, Gilbert DT, (2010) "A wandering mind is un unhappy mind", Science, Nov 12, 330 (6006):932,
- Madrigal, A. 2009. Don't Tell Geico: You May Be a Natural Born Bad Driver. WIRED. Available at: http://www.wired.com/wiredscience/2009/10/genetically-baddriving/
- SA McHughen, PF Rodriguez, JA Kleim et.al., 2010. BDNF Val66Met Polymorphism Influences Motor System Function in the Human Brain, Cerebral Cortex 20(5), 1254-1262
- Minskey, M.: The Emotion Machine, Simon & Schuster (2006) (Takebayashi, Y. (trans), Hakase-no nou-no tanken -joushiki kanjuo jiko toha-, Kyoritsu Shuppan (2009)).
- Panksepp, J.; and Biven, L. 2012. *The Archaeology of Mind: Neuroevolutionary Origins of Human Emotions*. London UK: W. W. Norton & Company, 379.
- Pecina, M., Mickey, B. J., Love, T., Wang, H., Langenecker, S. A., et al. 2012. DRD2 Polymorphisms Modulate Reward and Emotion Processing, Dopamine Neurotransmission and Openness to Experience. *Cortex* 49:877-890.
- Perry, J. ed. 2008. *Personal Identity*. Oakland, CA: University of California Press.
- Picard, R. W. 2000. Affective Computing. Cambridge, MA: The MIT Press.
- Rafael A. Calvo and Dorian Peters, (2014) "Positive Computing Technology for Wellbeing and Human Potential-", The MIT Press.
- Reuter M, Frenzel C, Walter NT, Markett S, Montag C. 2011. Investigating the genetic basis of altruism: the role of the COMT Val158Met polymorphism. Soc Cogn Affect Neurosci. Oct;6(5):662-8.
- Russell, D, Peplau, L. A.. & Ferguson, M. L., (1978) "Developing a measure of loneliness". Journal of Personality Assessment, 42, 290-294..
- Rostami, E., Krueger, F., Zoubak, S., dal Monte, O, Raymont, R., Pardini, M., Hodgkinson, C.A., Goldman, D., Risling, M., Grafman, J. 2011. BDNF Polymorphism Predicts General Intelligence after Penetrating Traumatic Brain Injury. *PLoS One* 6(11): e27389.
- Saphire-Bernstein, S., Way, B. M., Kim, H. S., Sherman, D. K., and Taylor, S. E. 2011. Oxytocin Receptor Gene (OXTR) is Related to Psychological Resources. In *Proceedings of the National Academy of Sciences in the United States of America*, 108(37):15118-15122.
- Smillie, L. D., Cooper, A J., and Pickering, A. D. 2011. Individual Differences in Reward-Prediction-Error: Extraversion and Feedback-Related Negativity. *Social Cognitive and Affective Neuroscience* 6(5):646-652.
- Swan, M. 2012a. Health 2050: The Realization of Personalized Medicine through Crowdsourcing, the Quantified Self, and the Participatory Biocitizen. *Journal of Personalized Medicine* 2(3):93-118.
- Swan, M. 2012b. Crowdsourced Health Research Studies: An Important Emerging Complement to Clinical Trials in the Public Health Research Ecosystem. *Journal of Medical Internet Research* 14(2):186-198.
- Swan, M. 2014. Next-Generation Personal Genomic Studies: Extending Social Intelligence Genomics to Cognitive Performance Genomics in Quantified Creativity and Thinking

Fast and Slow. In The Association for the Advancement of Artificial Intelligence 2013 Spring Symposia: Data Driven Wellness: From Self-Tracking to Behavior Change.

Swan, M. 2016. The Future of Brain-Machine Interfaces: How to feel comfortable joining a Cloudmind Collaboration. *Journal of Evolution and Technology*. In review.

Szuhany, K.L., Bugatti, M., Otto, M.W. 2015. A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *Journal of Psychiatric Research* 60:56-64.

Takebayashi, Y., (2014) Artificial intelligence technology for assisting patient's life with dementia. The Journal of the Japanese Society for Artificial Intelligence. Volume 29, Number 5, pp. 515-523,

A Terracciano, S Sanna, M Uda, B Deiana, G Usala, F Busonero, et al., Genome-wide association scan for five major dimensions of personality, *Molecular psychiatry* 15 (6), 2010, 647-656

Wigner, E. 2006, 1959. The Unreasonable Effectiveness of Mathematics in the Natural Sciences. *Communications on Pure and Applied Mathematics* 13(1):1-14.

van Winkel, M., Peeters, F., van Winkel, R. Kenis, G., Collip, D., Geschwind, N., Jacobs, N., Derom, C., Thiery, E., van Os, J., Myin-Germeys, I., Wichers M. 2014. Impact of variation in the BDNF gene on social stress sensitivity and the buffering impact of positive emotions. *Eur Neuropsychopharmacol*. 24(6):930-8.