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Problems with Models in Psychiatry

Over the past decade or two, psychiatry has largely adopted scientific ways. Due to intellectual and budgetary pressure, operational diagnoses and randomised trials now prevail. These methods are demonstrably reliable and useful; but often appear far removed from clinical practice, where patients need to be treated as individuals, and idiosyncratic details can be the key to therapeutic success. There are continuing concerns about the failure of research methods to convincingly capture such complexity (Nunn et al. 2000; Szasz 2001; Timimi 2004; reviewed by Kandel 1998; and Midgley 2004). This essay argues that bridging the gap requires researchers not just to incrementally improve models of mental function, but to become far more rigorous in the ways we create and use such models.

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Here we are using the term model as a convenient shorthand for simplifications of reality. In order to focus on science rather than philosophy, we include the related concepts of theory, hypothesis, paradigm, picture, representation, and simulation. We exclude models that are not simplifications, such as simulations of every molecule in a synapse, and animal models that are not simplifications in their target area. But all animal models in psychiatry are dramatically simpler than the group of people with a disorder, in homogeneity, cytoarchitecture, upbringing, and cognition (see e.g. Moore 2004).

Every thought and every perception involves at least one model: the world we perceive is constructed from our sensations and our experience. In science, every hypothesis is based on a model. In clinical work, every treatment decision is based on models of the patient and his environment; and the fitting of these to models of disorders and treatments. Thinking is impossible without models.

There are at least twenty reasons why psychiatrists need to simplify (Meehl 1978); and many ways to do this. Some are explicit: Freud's topographical model; neuropsychological models; animal models; computational models (which can mean models of how information is processed, or models implemented on a computer). We add another kind of model, namely the unspoken simplifying assumptions made by all practitioners. The kinds of models differ in many ways, and are usually considered separately but, in the spirit of Synergies we group them together. This approach will frustrate readers concerned with just one class of models, but we hope that the approach will improve the understanding of results

from models; encourage cross-fertilisation between nosological, psychological, animal, and computational communities; and perhaps clarify the underlying real-world phenomena.

Problems with models themselves

Being too simple

Although an evolutionary drive to simplicity does exist (Azevedo et al. 2005) it does not appear to be a major force (Kirschner and Gerhart 1998). Many real biological mechanisms are much more complicated than might be expected, in genetics and biochemistry, cognition and ecology. "The 'typical' behaviour of complex systems is often quite simple, so that a naive view leads to simple models and (wrong) explanations of most phenomena." (Carlson and Doyle 2001; see Williams and Taylor 2004; and Peterson and Flanders 2002).

Dozens of neuropsychological abnormalities, and at least 7 genes, have been found to make a contribution to some cases of Attention Deficit / Hyperactivity Disorder (ADHD). The true tally must be much greater, given the thousands of interacting genes that govern brain function, versus the small number of named neurodevelopmental disorders. This makes it impossible for a simple computational framework, or a single strain of rats, to capture all facets of a disorder. Current models of ADHD need to be reconceptualized as models of individual processes contributing to ADHD, so the set of all current ADHD models becomes the set of interacting ingredients to be incorporated into a more comprehensive ADHD model.

Endophenotypes are generally defined as genetically determined, fairly hidden traits that underlie disorders. But some definitions require that the endophenotype be specific to a disorder – problematic when many risk factors are shared between disorders. Others have required that endophenotypes be discrete types, rather than graded – which would make them very unusual in psychology, and would in practice largely restrict the term to effects of single alleles. These restrictive definitions are natural by-products of underlying models. A danger is that they result in psychiatric research being over-focussed so that important patterns are missed.

Information has a deep mathematical and computational underpinning, which is incorporated into very few psychiatric models, even though brains clearly process information and psychiatric diagnoses are most often based on what patients say. This omission has three causes: (a) definitions of disorder, which underemphasise learned factors contributing to illness; (b) the vague view that pharmacological treatments normalize chemical imbalances linked to psychiatric disorders; and (c) the difficulty of including information processing concepts (see Dayan and Abbott 2001). The omission probably leads to an undervaluing of the importance of psychological and social interventions. It seems likely to be superseded.

Being too powerful

This problem happens when a model is vague or insufficiently specified, so there is no way to weigh its relevance, or to disprove it. Nonquantitative, nonbiological models based on verbal reasoning are particularly at risk. In the extreme case, a model can account for any possible finding; obvious examples are belief in God or the Devil. After a

century of development, the wealth of described psychodynamic processes are adequate to describe essentially any clinical situation in several ways (Meehl 1998). This can be useful clinically, but the internal consistency of formulations can also create an illusion of correctness. Psychodynamic theory is difficult to test or to relate to neuroscience, but this may change (Kandel 1998).

Risky predictions (i.e. both unlikely and testable) are an important means of testing models (Popper 1959), and are hardly seen in psychiatry. Of course, predictions only test a model to the extent they were previously unexpected: predicting a new cognitive deficit in a highly deficit-enriched group carries very little risk. As another example, simple feedforward neural net models are able to copy essentially any empirical input-output mapping; therefore, their ability to copy a particular mapping tells us almost nothing about brain structure or function.

Being unidisciplinary

The biggest obstacle to psychiatric progress is its unidisciplinary nature (Kandel 1998), and one of the greatest strengths of explicit models is that they encourage interdisciplinary work. Unfortunately many researchers and clinicians are so focused on their own models that they don't compare them to others, and don't adequately disseminate, or integrate, the results.

Being too complicated

Complexity increases the likelihood of many types of logical errors (Gilovich 1993). Complex interactions between processes can be studied using computer simulation. Such simulation is itself complicated, often producing unexpected emergent properties that need to be understood in order to be published or (much more often) debugged. Simulation has several compensations for the effort involved, though, including repeatability, modifiability, distributability, and the facility to produce graphs that communicate to noncomputational readers. This is important because complex presentations can lead to audience rebellion – or can seduce by distracting from the core issues. When models are too complex to be understood in one sitting or one article, they need to be presented in pieces.

Problems with the ways models are used

Having a model without acknowledging it

Clinicians and researchers often overlook the fact that the disorders they work with are themselves models, constructed by committees of experts. For example, the successive versions of the Diagnostic and Statistical Manual (DSM) are intended eventually to become a comprehensive catalogue of disorders, in which the disorders are "natural kinds" (Zachar 2000) created by carving nature at its joints. This may be an impossible task, because there is no evidence for such joints in mental function, within or near ADHD (Figure 1).

The idea that the most severe cases, being closest to a prototype, have the most in common, is another unspoken model that has been central to clinical and research work. Research has often focused on combined type ADHD, or the even more severe hyperkinetic disorder, for this reason. Similarly, formal diagnostic systems usually include a threshold number of

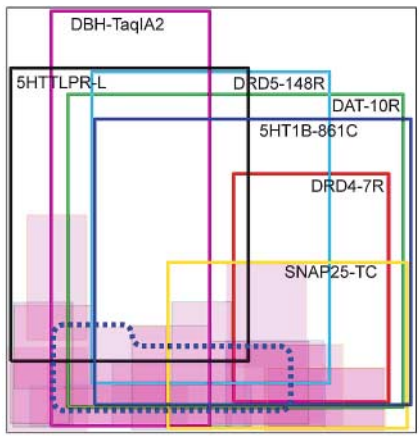

Figure 1. One possible population distribution of genes contributing to ADHD. ADHD individuals are within the dotted outline. The size of named rectangles indicates actual allele frequency; 20 unnamed ones, each conferring 20% increased risk in 5% of the population are hypothesized based on non-replications in genetic studies. Interactions of alleles are unknown so arrangement is derived by optimising individual and combined (additive) odds ratios, together with the normality of the resulting risk distribution.

symptoms. This is completely appropriate if a very damaging "core" problem is often combined with unrelated or ameliorating factors that confuse the picture. However, genetic and behavioural research have not yet revealed a dominant core (Bobb et al. 2004; see Rapport et al. 2000), and it is possible that high thresholds select patients who individually have several smaller problems, rather than the single core that was originally hoped for. Figure 1 illustrates this for risk alleles; a similar diagram could presumably be made for neuropsychological risk factors.

The concept of disorder is itself based on unstated models of humanity, in which people are generally intelligent, predictable, and sociable, and in which deviations from this are flaws (see Szasz 2001). Society's reluctance to stigmatise these flaws, and optimism based on past medical progress, have led the deviations to be called disorders, with the implication that it is only a matter of time before they can be "treated". At CAS, we have made simulations that cast doubt on such a view of impulsivity, showing that in certain conditions, group survival can be enhanced by having a minority of unpredictable individuals. ADHD behaviours may have some value to society simply because they are different from average behaviours.

Using a model for the wrong purpose

Many people expect that there is a single best way to parcel or understand the world, and that since biological measurements are so obviously right, they must be it. However, just as molecules and signals can most obviously be grouped topographically (shown in the left cylinder of Figure 2), they can also be grouped according to other principles (shown in the other cylinders) (Killeen 1999; Dayan and Abbott 2001; Olds 2000). The hierarchies of formal processes and information processing are just as real as the visible brain, but tend to be neglected.

Descriptive models do not link levels, but are often wrongly treated as explanations, which do (Figure 2). For example, fitting equations to data points, which has a rich and productive history from Ptolomy to Herrnstein, is useful for prediction but sheds essentially no light on underlying mechanisms. Most diagnostic systems such as DSM consider a single level (high in the third column of Figure 2). They help to make epidemiology and treatment reliable, but they have come to be used as the basis for almost all research in biological psychiatry, for which they are much

less appropriate. Similarly, psychodynamic formulations describe high-level processes, so direct links to biology may be as difficult (and irrelevant) as explaining WORD bugs in terms of computer hardware.

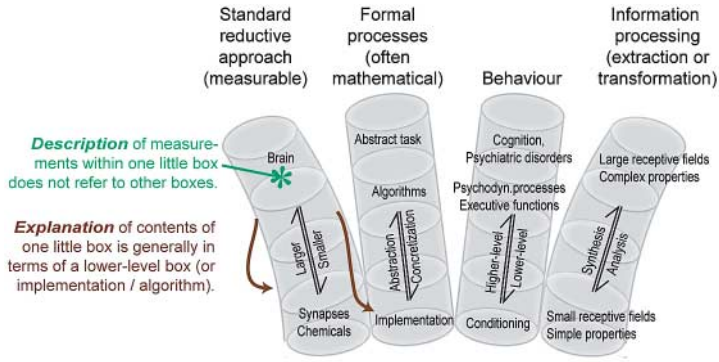

Figure 2. Hierarchies within biological information-processing systems. Models can address any parts of these hierarchies. The lowest levels of the hierarchies are closely bound together; higher up, connections become much more tenuous.

In order for multi-level explanations to be grounded in reality, they need to be based on a painstakingly acquired understanding of low-level connections between the biological and informational worlds. This implies studying genetically identified endophenotypes (e.g. Caspi et al. 2003) rather than high-level concepts such as theory of mind; and single standardizable interventions rather than months of individualised therapy.

Having a model of the wrong thing

Throughout history, treatments have been used as models of disorder, and vice versa. The following line of reasoning has been very influential: 'Since stimulants are a very effective treatment for ADHD, and stimulants affect dopamine, ADHD is primarily a dopamine disorder.' The reasoning is much weaker than it appears, because (a) stimulants help human controls who don't have ADHD; (b) stimulants don't help all aspects of ADHD; (c) after brain damage, stimulants help both humans and rats; (d) stimulants affect other transmitters beside dopamine.

Not realising how the model affects your reasoning

Having a model, especially a personal one, can influence thinking in many ways (Gilovich 1993). For example, it increases our interest in data that supports the model, but not our interest in whether other models exist that are supported by the data. Being aware of such cognitive biases can help to reduce them.

Requiring inappropriate competition between models

According to Occam's principle the simplest explanation is the best. But this doesn't help us choose between the many models of ADHD, for example, which are all similarly simple. Platt suggested that we use "strong inference", relying on crucial experiments to choose between alternative models (Platt 1964). Alternatively, models can be made to compete quantitatively to find which provides the best balance between simplicity and data-fitting (Burnham and Anderson 2002). But these ideas have limited

applicability to the hyper-multifactorial problems that are common in biology (Kendler 2005; Carlson and Doyle 2001). This is because there is no agreed set of data to fit; and no fully integrated model of ADHD.

Not documenting weaknesses in the model

Like tents, models need well-spaced supports. A model with supportive evidence from behaviour, genetics, and drug effects is far stronger than one with behavioural support alone – such as most psychodynamic or behaviourist models. Compared with the main supports, clear boundaries are much less exciting to establish: the tent pegs of the modelling world. But without them, all models lose credibility, because common sense dictates that models are not all right, all the time. Beyond the pegged area, discrepancies need to be documented, to clarify the relationship between the model and reality.

Conclusions

Progress toward understanding the roots of psychiatric disorder depends on the methodical construction of integrated computational models, which will in turn require close collaboration between clinicians, neuroscientists, psychologists, and computationalists. Only such integrated models can sensibly compete against each other. Real effort is needed to avoid oversimplifications and preconceptions.

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References

Azevedo, R. B., Lohaus, R., Braun, V., Gumbel, M., Umamaheshwar, M., Agapow, P. M., Houthoofd, W., Platzer, U., Borgonie, G., Meinzer, H. P., and Leroi, A. M. (2005). "The simplicity of metazoan cell lineages." Nature, 433(7022), 152–156.

Bobb, A. J., Castellanos, F. X., Addington, A. M., and Rapoport, J. L. (2004). "Molecular genetic studies of ADHD: 1991 to 2004." Am. J. Med. Genet. (Neuropsych. Genetics).

Burnham, K. P., and Anderson, D. R. (2002). "Model selection and multimodel inference: A practical information-theoretic approach." Springer-Verlag, New York.

Carlson, J. M., and Doyle, J. (2001). "Robustness and complexity." Robustness in Natural, Engineering, and Social Systems,(RS-2001-017).

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., McClay, J., Mill, J., Martin, J., Braithwaite, A., and Poulton, R. (2003). "Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene." Science, 301(5631), 386–389.

Dayan, P., and Abbott, L. F. (2001). "Theoretical Neuroscience." MIT Press.

Gilovich, T. (1993). "How we know what isn't so: the fallibility of human reason in everyday life." Free Press, New York.

Kandel, E. R. (1998). "A new intellectual framework for psychiatry." Am. J. Psychiatry, 155, 457–469.

Kendler, K. S. (2005). "Toward a philosophical structure for psychiatry." Am. J. Psychiatry, 162(3), 433–440.

Killeen, P. R. (1999). "Modeling modeling." J. Exp. Anal. Behav., 71(2), 275–280.

Kirschner, M., and Gerhart, J. (1998). "Evolvability." Proc. Natl. Acad. Sci. U. S. A, 95(15), 8420–8427.

Meehl, P. E. (1998). "The Power of Quantitative Thinking." (Speech on receipt of J. M. Cattell Award at Am. Psychol. Society,Washington DC, 23 May).

Meehl, P. E. (1978). "Theoretical Risks and Tabular Asterisks: Sir Karl, Sir Ronald, and the Slow Progress of Soft Psychology ." J. Consult Clin. Psychol., 46, 806–834.

Midgley, N. (2004). "Sailing between Scylla and Charybdis: Incorporating qualitative approaches into child psychotherapy research." J. Child Psychotherapy, 30(1), 89–111.

Moore, B. R. (2004). "The evolution of learning." Biol. Rev. Camb. Philos. Soc., 79, 301–335.

Nunn, K., Nicholls, D., and Lask, B. (2000). "A new taxonomy." Clin. Child Psychol. Psychiatry, 5(3), 313–327.

Olds, D. D. (2000). "A semiotic model of mind." J. Am. Psychoanal. Assoc., 48(2), 497–529.

Peterson, J. B., and Flanders, J. L. (2002). "Complexity management theory: motivation for ideological rigidity and social conflict." Cortex, 38(3), 429–458.

Platt, J. (1964). "Strong Inference." Science, 146(3642), 347–353.

Popper, K. R. (1959). "Conjectures and Refutations: The growth of scientific knowledge." Routledge, New York.

Rapport, M. D., Chung, K. M., Shore, G., Denney, C. B., and Isaacs, P. (2000). "Upgrading the science and technology of assessment and diagnosis: laboratory and clinic-based assessment of children with ADHD." J. Clin. Child Psychol., 29(4), 555–568.

Szasz, T. (2001). "Mental illness: psychiatry's phlogiston." J. Med. Ethics, 27(5), 297–301.

Timimi, S. (2004). "Rethinking childhood depression." BMJ, 329(7479), 1394–1396.

Williams, J., and Taylor, E. (2004). "Dopamine appetite and cognitive impairment in Attention-Deficit / Hyperactivity Disorder." Neural Plasticity, 11:1-2.

Zachar, P. (2000). "Psychological Concepts and Biological Psychiatry: A Philosophical Analysis." Adv. Consciousness Research, Series A, 28.