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opinion & debate

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Psychotherapy meets neuroscience

A more focused future for psychotherapy research

The 'evidence base' for my contribution to futurology is a set of integrative reviews of outcome studies of psychotherapy on which I have collaborated with a number of colleagues (Roth & Fonagy 1996; Fonagy *et al*, 2002*a*,*b*). This work is a pleasure, not so much because of the enlightenment that reading hundreds of papers provides, but rather because of the technical challenges that compiling material across broad fields invariably presents.

Looking into the future often initiates an appraisal of the past. At the risk of making implausibly broad generalisations, here are three observations concerning the limitations of the intensive research into psychotherapy outcomes over the past 3 decades. First, we know precious little about who is likely to benefit from what type of therapy; we know about some protocols that work, and can perhaps make generalisations about new protocols that are likely to be successful for particular diagnostic groups, but the literature is not very informative about clinically important choice points on pathways of care. Second, for many disorders a range of psychological approaches appear to be somewhat effective, but in most instances these therapies are made up of a collection of interventions of varying specificity. Further, the observed effects are rarely correlated with changes in putative mediating processes, making unequivocal causal attributions hazardous (e.g. Farmer *et al*, 2002). Third, psychotherapy researchers and practitioners, alike become attached to methods which they advocate in sometimes quite business-like ways, leading to rapid 'guildification' of even recently developed interventions (e.g. Linehan, 1993; Henggeler *et al*, 1994), not unlike the tragedy that befell psychoanalysis.

The psychotherapy research of the future will have to be more firmly rooted in developmental psychopathology. We increasingly appreciate that psychiatric disorders of adulthood are rooted in abnormalities already observable in childhood or adolescence (e.g. Kim-Cohen *et al*, 2003). There will be a merging of (developmental) psychopathology and psychotherapy research. It is likely that the elucidation of pathogenic mechanisms – essential for the development of effective and specific psychological interventions (Kazdin, 2003) – will only be achieved through developmental observations. The structured, manualised psychotherapy techniques of the future will be designed to specifically address empirically established developmental dysfunctions. Future psychotherapy trials will be increasingly seen as the only viable experimental tests of rival psychosocial aetiological models of personality (e.g. Hudson *et al*, 2002; Toth *et al*, 2002).

The value of well-targeted psychotherapy treatment outcome studies in modifying our model of psychopathology is well illustrated by early prevention programmes (see Howe *et al*, 2002). A report of a 20-year follow-up of an educational and physical enrichment programme showed that those who were demographically at high risk who underwent the programme manifested less schizotypal behaviour and lower levels of interpersonal deficits (Raine *et al*, 2003).

In addition to the 'guildification' and non-specificity of much current psychotherapy research, the measures of outcome used in many trials leave room for improvement. Most self-report measures in standard use are oriented towards symptom distress, and are of greatest relevance to trials of pharmacological products designed to address specific psychiatric symptoms. The virtual absence of user involvement in the devising of these measures has been a flaw in this approach. There is a significant risk that the evidence base we compile for psychotherapy will be almost uniquely shaped by professional priorities rather than by criteria important to users. Whereas the former have symptom distress at the core of all their systems, following the Ohio research (Crane-Ross *et al*, 2000; Roth Crane-Ross, 2002), we know that this may be by no means the most important concern of most service users, who worry far more about housing, employment and the presence of supportive companions. Most outcome measures are prone to bias and are potentially highly reactive (Sechrest *et al*, 1996), It is a striking and probably not unrelated fact that 70–80% of the variability in outcomes across studies can be predicted from the theoretical allegiance of the investigators (Luborsky *et al*, 1999).

Non-biased, non-subjective measures of outcome are urgently required. Neuroscience (particularly brain imaging) will deliver this sooner rather than later. Psychoneurobiology research is identifying neural correlates of complex subjective states (Adolphs, 2003), for example the experience of social exclusion (Eisenberger *et al*, 2003) or concern about the mental states of another person (Frith & Frith, 2003). There are indications that scanning techniques that allow the simultaneous imaging of two individuals interacting (Tomlin, Montague & King-Casas, Personal Communication, 2004) will be able to offer unbiased indicators of relationship quality as this changes as a consequence of psychological therapy.

The greatest contribution of neuroscience to psychotherapy research is likely to be through progress in molecular biology. As molecular genetic findings unfold over the next few years, it is likely that biological vulnerability will become increasingly detectable; although single genes and polymorphisms will probably never account for a large proportion of variability, combinations of genes may increasingly identify specific

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types of environmental vulnerability (Plomin & McGuffin, 2003). To give just one example, the promoter region of the serotonin transporter gene (*SLC6A4*) is involved in reuptake of serotonin at brain synapses; in the gene-linked polymorphic region, the short (S) allele has a lower transcription efficiency than the long (L) allele. There is inconclusive evidence on direct association with depression (Lesch, 2004). However, an analysis of the Dunedin longitudinal sample has dramatically demonstrated that in the presence of three or more life events the likelihood of a diagnosis of major depression for those with the S allele increases from 10% to 28–32%, whereas in those with the L genotype the risk of an episode of major depression is 10–16% regardless of life events (Caspi *et al*, 2003).

This discovery may create important opportunities for targeting prevention interventions at those with the S genotype. It is not yet clear what aspects of life events might represent a depressogenic effect to those with the S allele. It might well be that enhancing the capacity of those with the S genotype to cope with adverse life events would reduce the potency of the underlying biological vulnerability to trigger major depression. The field of mental illness prevention, although impeccable in its logic, has always had difficulty in appropriately targeting preventive interventions when demographic data were the sole guide to identifying the indicated group. The rationale for enrolling a large number of individuals into prevention programmes who are unlikely ever to develop the problem has often led to selective uptakes and prevented a genuine test of the prevention approach (Beardslee *et al*, 2003).

Preventive efforts will be enhanced by having powerful biological indicators of environmental vulnerability, so that individuals can appreciate that reducing the impact of specific types of environments will protect them from the disease process.

The true importance of molecular biology in this context, however, is in opening a vista of biologically indicated psychosocial treatments – not just preventions. As we begin to understand the causal path that disease processes follow in the vulnerable brain, the need for specific psychosocial treatments to assist individuals with these vulnerabilities will become acute. Knowing that in individuals with the S/S genotype severe maltreatment doubles the probability of major depressive disorder (to over 60% from 30% for those with the genotype) helps us to focus interventions on childhood maltreatment for the first group to a greater extent than for the L/L group. It would be fascinating to know whether severely maltreated individuals with these genotypes give different weights to this experience with respect to their disorder. The psychotherapy would be designed to help these individuals to circumvent and, if possible, reverse the impact of this type of psychosocial event on brain function.

Future psychotherapy research must entail the removal of the opposition between psychosocial and biological perspectives. As we identify specific brain dysfunctions associated with psychological disorders, the need for psychotherapy will become greater – not less, as some fear and others advocate. Pharmacological interventions specific to the underlying cause of brain dysfunction particular aetiology associated brain dysfunctions will be a long time coming. So far, there is little evidence that genotyping can indicate the choice of psychotropic medication (e.g. Solvason *et al*, 2003). Psychological approaches, in contrast, can be developed and tested rapidly. Psychotherapy can be available to provide a 'work-around', a set of techniques that the mind can use to overcome a biological deficit. This is not to suggest that psychotherapy could be to the brain as physiotherapy is to the healing of the musculoskeletal system (although this would be nice if true), but rather that the human mind as a system evolved to be able to bypass and overcome dysfunctions in the physical organ upon which it depends: the brain. It was to exploit this self-healing capacity that Freud invented psychotherapy. Increased neuroscientific knowledge will help us to help the brains of our patients to devise and make use of sometimes complex and sometimes simple mental strategies to cope with weaknesses in their brain function, whether these are caused by genetic vulnerability, developmental assault or a unique combination of the two.

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