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1. METHODS TO STUDY GENETIC AND ENVIRONMENTAL CAUSES OF BEHAVIOUR

- 1.1. Introduction
- 1.2. Twin studies
- 1.3. Adoption studies
- 1.4. Blended families design
- 1.5. Natural experiments
- 1.6. Migration designs
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1.1. INTRODUCTION

The question of whether a behaviour is caused by genes or the environment is seen as too simplistic today. But there is still interest in trying to explain the differences between individuals on a behaviour in terms of how much is genetic and how much is environmental caused.

However, Rutter et al (2001) observed: "The complexities of nature-nurture interplay involved in multi-factorial causation do not mean that we should be content with a general assumption that life is complicated and that causal processes involve varying mixtures of genetic and environmental risk factors... [because] although the research challenges are severe, the future prospects for causal research into environmental risk factors are very good" (p315 & p316).

1.2. TWIN STUDIES

Twins are highly sought after by researchers in the gene-environment debate. There are a number of different ways to study twins.

1. MZ apart.

Identical (monozygotic; MZ) twins share all of the same genes, and if they are raised apart (or one twin experiences a major event that the other does not), any difference between them is seen as due to the environment. But there is only a limited number of such twin pairs.

Twin studies depend on volunteers, and they may have been separated at any age, and the environments may not be that different. Bronfenbrenner (1986) reported correlation rates of 0.86 for particular behaviours when the "MZ apart" were reared in similar environments, and 0.26 when in different environments.

2. MZ vs DZ.

Most commonly MZ and DZ (dizygotic; non-identical) twins are raised in the same family. The concordance rate of the twin pairs can be calculated. This is the likelihood of the second twin showing the same behaviour as the first twin does. So a concordance rate of 100% (or 1.00) would mean that both twins show the behaviour in question. A comparison can be made of the concordance rates of MZ and DZ twins, and if the former is higher, the extra amount is taken as due to genetics.

3. Extended twin-family design.

This design includes siblings, spouses, and parents of twins.

The advantage over the classic twin design is the ability to measure the shared environment effect (Rutter et al 2001). Furthermore, including the parents of twins can provide information about cultural transmission from parents to offspring (Distel et al 2009).

For example, Distel et al (2010) recruited 4818 twins from the Netherlands Twin Register and the East Flanders Prospective Twin Survey with 817 of their siblings (308 brothers/509 sisters), 1350 fathers and 1698 mothers for a study of loneliness. The researchers found that loneliness was "moderately heritable".

While Distel et al (2009), for a study of borderline personality disorder, recruited 5017 twins, 1266 siblings, 3064 parents, and 939 spouses from the same sources in Holland and Belgium.

4. Offspring of twins design 1.

This research design compares the offspring of identical twins. The child shares half the genes of the mother, say, but in the case of MZ twin parents, the child also shares half the genes of the aunt. This can be viewed as a control for the genetic effect, and any difference between the child of the twins must be due to the environmental influence of the parent. Or put another way, if a behaviour is genetic, the child should correlate with it's parent and parent's MZ twin on that behaviour (Rutter et al 2001).

For example, Duncan et al (2008) investigated the development of cannabis abuse and dependence in adolescence and young adulthood after child abuse (physical and sexual) (environmental factor) and/or

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¹ "Pseudo-adoption study" (Duncan et al 2008).

having a father with drug dependence (genetic factor) using US military veterans data. There were four groups of participants:

- i) High genetic/high environmental risk Children raised in households where fathers had drug dependence.
- ii) High genetic/low environmental risk Children raised in households where the father did not have drug dependence, but the father's MZ twin did (ie: uncle).
- iii) Moderate genetic/low environmental risk Children raised in households where the father did not have drug dependence, but the father's DZ twin did.
- iv) Low genetic/low environmental risk Neither father nor twin had drug dependence.

It was found that exposure to child sexual abuse (but not physical abuse) was associated with cannabis abuse/dependence compared to no childhood abuse after controlling for genetic factors. In the first group above, 72% of offspring were diagnosed with cannabis abuse or dependence compared to 8% in the second group. Because the genetic risk component is controlled between both groups, any difference is due to environmental factors.

5. Twin-singleton comparisons.

The comparison of twins raised together and single offspring can be made in relation to a particular behaviour. There will be differences in the womb (two sharing vs one) as well as in family interactions (a parent with two twins - trio vs a parent and child - dyad). Twins are more likely to experience premature births, low birth weight, and the family stress of multiple births (Posthuma et al 2000).

Most studies compare unrelated singletons with twins ², but Posthuma et al (2000) studied families that had a pair of twins and another single child in the Netherlands. No difference was found between the adult twins and their non-twin siblings on intelligence measures.

In rare cases, comparison of singletons with twins where one twin dies shortly after birth can show the effect of the womb environment (eq: Record et al 1970).

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² For example, Record et al (1970) found an average of 4.4 IQ points lower for twins than singletons.

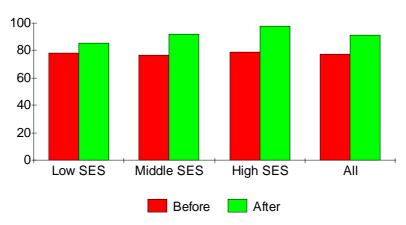
1.3. ADOPTION STUDIES

In the search for the effect of genes on behaviour as opposed to the effect of the environment, adoption studies can be used because the genetic element is "removed". Children raised by non-genetically-related adopted parents who show the behaviour of interest must have developed it due to the environment.

But offspring can be affected during their time in the womb by the environment or mother's behaviour (eg: smoking in pregnancy). Furthermore, the age of adoption after birth is also important.

Adopted parents are not typical of the general population because of who volunteers to adopt, and that adoption agencies tend to screen out potential applicants viewed as high-risk (Rutter et al 2001).

One example shows the effect of the type of adopted environment on intelligence. Duyme et al (1999) looked at 65 neglected or abused children in France removed by court order from the biological families (between 1970 and 1978) and placed with adopted families between the age of 4 to 6 six years old. The mean IQ of all the children at the point of adoption was around 75 points. The adopted families were divided into low, middle, and high socio-economic status (SES) ³. By the follow-up in adolescence, the twenty-four children adopted by low-SES families had gained an average of 7.7 IQ points, while this was 15.8 points for the twenty-two children with middle-SES families, and 19.5 for high-SES families (figure 1.1).



(Data from table 1 p8792 Duyme et al 1999)

Figure 1.1 - Mean IQ before and after adoption.

³ SES based on adoptive father's occupation - high-level manager or professional (high), middle and lower level managers, tradesmen or craftsmen (middle), and unskilled workers (low).

An alternative method is to compare siblings where one child is adopted and the other stays with the biological family. For example, Schiff and Lewontin (1986) reported that the adopted siblings (raised in more favourable environments) had an average IQ of twelve points more than the siblings who remained.

Adopted children can also be compared to children reared in institutions. If the children are comparable (ie: all taken into institutional care initially), then the comparison is actually between those who remain in the institution and those taken by individual families. The focus is upon the influence of the environment. But comparisons may be limited by certain factors:

- Choice of child to adopt "better" children chosen leaving "worse" children in the institution (ie: groups not equal) or random allocation (ethics).
- Bias in assessment ie: researchers know who is adopted and who not.
- Confounding variables eg: differences in schools attended.
- Continuity/discontinuity some child may be moved to different families which leads to a discontinuity in care.

1.4. BLENDED FAMILIES DESIGN

The growth in divorce and re-marriage in recent years has given researchers another method for studying genes and environment, the blended families design. Blended and step-families will contain full, half, and genetically unrelated siblings reared in the same family (Rutter et al 2001).

1.5. NATURAL EXPERIMENTS

The effect of the environment on behaviour can be studied with natural experiments of children who experience major change or events in their lives. These are naturally occurring events that the researchers take the opportunity to study.

i) Schooling experience - eg: children who miss large amounts of schooling due to war. De Groot (1951) reported an average IQ of five points less among children whose schools were closed in Holland during World War II when compared to pre-war children.

ii) Moving - eg: children moving from a high-crimerisk area to a low-risk one and their anti-social behaviour (Osborn 1980). Using data from the Cambridge Study in Delinquent Development which follows a group of boys from inner city area of south London since the 1960s. At twenty-one years old, 57.5% of those who had remained in London had convictions compared to 37.3% of those living outside London. Furthermore, males who had a criminal record were less likely to re-offend if they moved out of London. But Osborn (1980) admitted that it was "not clear whether this was because of changed behaviour patterns or because of other factors associated with living out of London, such as differences in police procedures and risks of detection" (p59).

1.6. MIGRATION DESIGNS

"Migration constitutes a potentially informative phenomenon because people take their genes with them when they move from one country to another, but often the migration entails a radical change in lifestyle. Accordingly, it provides a natural experiment in which the role of environmental effects can be assessed by determining the effects of the change of environment" (Rutter et al 2001 p310).

The behaviour by the migrant can be compared to the behaviour of the general population in the country of origin, and any difference can be due to the differences in environment of the two countries ⁴. The migrant can also be compared to the indigenous general population. A good example of the use of this method is the rates of mental illness among migrants.

Even better for controlling genetic difference would be siblings where one migrates and the other does not, or best of all, MZ twins who do this.

Individuals migrate for many reasons varying from economic advantage to escape persecution, so they may not be comparable with the general population in their home country (Rutter et al 2001).

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⁴ However, this assumption is challenged where the two countries are not that different, where the experience is similar in both countries (eg: deprivation), or where migrants maintain many aspects of their home culture (Rutter et al 2001).

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2. THE BENEFITS OF FEAR AND TOO LITTLE OF IT

- 2.1. Appropriate fear?
- 2.2. Too little fear
- 2.3. Appendix 2A Recognising facial expressions 2.3.1. Facial feedback hypothesis
- 2.4. References

2.1. APPROPRIATE FEAR?

Fear in appropriate situations has the evolutionary benefit of keeping the individual away from dangers and alive. It has been suggested that fear for certain animals, like snakes, is innate (or "prepared"; ie: biologically predisposed) (Bennett-Levy and Marteau 1984).

Research has shown that reaction times are faster for biologically relevant threats than non-threatening stimuli. For example, Ohman et al (2001) asked participants to respond as quicker as possible if a target picture was present among a number of stimuli. In one condition, a fear-relevant target (eg: picture of snake) was among four or nine pictures of fear-irrelevant stimuli (eg: pictures of flowers), and in the other condition, the other way around. Participants were quicker to spot the fear-relevant target among the fear-irrelevant stimuli than the fear-irrelevant target among the fear-relevant stimuli. When participants who had a fear of spiders or snakes were used, their reaction times in spotting that target was even quicker, but there was no difference for non-feared targets.

Flykt and Caldara (2006), using first year psychology students at the University of Geneva in Switzerland, divided them into spider-fearful, snake-fearful, and non-fearful groups (of nine participants each) based on their replies to a questionnaire about fears. In each trial, nine pictures were presented, and the task was to find either a snake picture among flower pictures, a snake among mushrooms, a spider among flowers, a spider among mushrooms, a flower among mushrooms, or a mushroom among flowers. The participants were instructed to press one button if the target was present and another button if absent. The fearful participants were quicker to spot their feared animal than to spot fear-irrelevant targets (table 2.1).

	SPIDER FEARFUL	SNAKE FEARFUL	NON-FEARFUL
Spider among flowers or mushrooms	760	894	798
Snake among flowers or mushrooms	822	772	857
Flower among mushrooms or vice versa	1004	1058	1057

(Source: Flykt and Caldara 2006 figure 1 p1082)

Table 2.1 - Mean reaction times (milliseconds) to spot target among other stimuli.

2.2. TOO LITTLE FEAR

Individuals who are the opposite extreme, and show no fear, are rare. Feinstein et al (2011) reported the case of a 44 year-old woman, SM, with damage to her amygdala, who appeared to show no fear.

Her fear reaction was tested in three different situations - a visit to an exotic pet shop with snakes and spiders, walking through a haunted house, and watching clips of scary films.

In the first situation, SM was spontaneously drawn towards the snakes and spiders, despite previously saying she "hated" them and "tries to avoid them". "When asked why she would want to touch something that she knows is dangerous and that she claims to hate, SM replied that she was overcome with 'curiosity'. The disconnection between SM's verbally stated aversion to snakes and spiders and her actual real-life behaviour was striking. She did not display any signs of avoidance, but instead exhibited an excessive degree of approach.." (Feinstein et al 2011).

The second situation involved a visit during Halloween to Waverly Hills Sanatorium, Louisville, Kentucky, USA, rated as one of the "most haunted" places in the world, where individuals were dressed as ghosts and monsters. "The hidden monsters attempted to scare SM numerous times, but to no avail. She reacted to the monsters by smiling, laughing, or trying to talk to them. In contrast, their scare tactics typically elicited loud screams of fright from the other members of the group. More than showing a lack of fear, SM exhibited an unusual inclination to approach and touch the monsters. Ironically, SM scared one of the monsters when she poked it in the head because she was 'curious' as to what it would feel like. Before, during, and after the haunted

house, SM was queried about her current level of fear. She never reported experiencing any elevations in fear, and her fear ratings were at 0 throughout" (Feinstein et al 2011).

Finally, SM was shown ten fear-inducing film clips along with clips to elicit emotions like sadness and happiness. Her subjective ratings of fear were very low (compared to the typical reaction - eg: one vs seven out of eight), but she showed the other emotions typically.

Generally, when completing questionnaires about fear, SM's scores were significantly lower than the mean scores for the general population.

SM's life history showed that she had experienced many fear-inducing situations in her life, like being held at knife point, and nearly being killed in an act of domestic violence. "What stands out most is that, in many of these situations, SM's life was in danger, yet her behaviour lacked any sense of desperation or urgency" (Feinstein et al 2011). She reported anger and upset about these events.

Feinstein et al (2011) concluded: "The unique case of patient SM provides a rare glimpse into the adverse consequences of living life without the amygdala. For SM, the consequences have been severe. Her behaviour, time and time again, leads her back to the very situations she should be avoiding, highlighting the indispensable role that the amygdala plays in promoting survival by compelling the organism away from danger... Indeed, it appears that without the amygdala, the evolutionary value of fear is lost" (p38). Furthermore, "the amygdala helps us navigate the fine boundary between approach and avoidance" (Justin Feinstein in Kloc 2011).

In another set of experiments, Adolphs et al (1995) found that SM's damage to the amygdala impaired the processing of fearful facial expressions (appendix 2A). But only because the damage was to both sides of the amygdala (bilateral) 5 .

The studies involved SM, six patients with unilateral damage to amygdala, and 12 patients with brain injury to other areas of the brain. The participants were asked to judge the facial expression in black and white photographs based on a choice of verbal labels given. Health controls were more than 80% accurate.

SM was as accurate as the other participants in recognising facial emotions, except for fear, which she failed to recognise.

⁵ In neuroimaging studies, the amygdala is seen to be activated when viewing facial expressions of fear, even subliminally (ie: outside conscious awareness) (Adolphs et al 1999).

But Hamann et al (1996) found contrary results - ie: no impairment in recognising the fear facial expression by individuals like SM. The difference in findings may have been due to differences in methodology between the studies - eg: whether labels for the facial expressions are provided or not by the experimenters, or how the emotional ratings were scored.

Adolphs et al (1999) reported a collaboration by different researchers to rectify the problem of methodological differences. Nine individuals with bilateral amygdala damage were studied, including SM (31 years old at the time). Sixteen individuals with brain damage, but not to the amygdala, from the Patient Registry of the University of Iowa were comparisons as were five healthy adults.

Participants were shown slides, one-by-one, of faces showing one of six emotions or neutral, and asked to rate each one from 0-5 on the six emotions (happiness, surprise, fear, anger, disgust, and sadness). The ratings were correlated with those of healthy individuals ("norm"). Thus, a correlation towards 1 shows agreement between the participant and the healthy individuals on the emotion shown by the face, while a correlation closer to 0 indicates that the participant's rating is different to the "norm".

The amygdala-damaged participants had a mean correlation close to one for happy faces, but less for all other faces with fear being the lowest (mean: 0.5). Individually, SM was the poorest at recognising fear (ie: lowest correlation), but there was some variation between the individuals in recognising fear.

2.3. APPENDIX 2A - RECOGNISING FACIAL EXPRESSIONS

The idea of "embodied cognition" suggests that the meaning of another's facial expression is perceived through unconsciously simulating the facial expression. The muscle movements feedback signals to the brain that aid the perceiver in understanding the emotion being shown on the face of the other person (Neal and Chartrand 2011).

If this is the case, individuals will become less accurate at perceiving facial expressions if their facial muscles are dampened, and more accurate when the facial muscles are amplified. Neal and Chartrand (2011) designed two experiments to test these predictions.

Experiment 1

This tested the idea that facial expression perception accuracy is reduced if the perceiver's facial feedback is dampened. The facial feedback is dampened

after Botox injections, which paralyse certain facial muscles by blocking acetylcholine release.

Sixteen women in the USA, who had undergone Botox injections for cosmetic treatment, were recruited for the research, and they were compared to fifteen women who had Restylane injections (dermal filler) for expression-related facial wrinkles. The participants were shown, one at a time, 36 black and white photographs of the eyes and surrounding area, and asked to rate the emotion from a choice of four adjectives. This is known as the "Reading the Mind in the Eyes" test (RMET) (Baron-Cohen et al 2001). The number of correct responses and the reaction time to answer were collected.

The mean accuracy of the Botox group was significantly lower than the Restylane group (70% vs 77% correct). There was no difference in reaction times between the two groups. "Thus, lowered accuracy in the Botox group could not be accounted for through differences in how quickly each patient group responded in the RMET" (Neal and Chartrand 2011). Botox reduced facial feedback, and thereby reduced the accuracy of facial emotion perception.

Baseline measures of accuracy were not taken before the Botox treatment. But the mean accuracy for adult female samples is about 76% (Baron-Cohen et al 2001).

Experiment 2

In this experiment, facial feedback was enhanced by the use of a gel that hardened (as in a face-mask) to produce resistance to facial muscle contraction. Half of the 95 participants had this gel applied to the face and half to the inner arm before the RMET. The former group were significantly better at the test (77% vs 72% correct). This supports the prediction that enhanced facial feedback improves perception of facial expressions in others.

2.3.1. Facial Feedback Hypothesis

Facial expressions show underlying emotional states, but could emotional states be the result of facial expressions? The facial feedback hypothesis (FFH), which has different versions, answers that question in the affirmative (Davis et al 2009).

The "necessity hypothesis" version of the FFH sees no emotional experience without facial feedback ⁶.

⁶ An emotional stimulus activates sub-cortical areas of the brain (below consciousness), which send signals to facial muscles (or receptors in the skin). These muscles contracting (or receptors activated) is fed back to the brain, and are consciously interpreted as emotions (Tomkins 1980).

However, this extreme view has been refuted. For example, Keillor et al (2002) reported the case of a woman (F.P) with total facial paralysis who experienced typical emotional responses to emotionally evocative photographs (table 2.2).

- 21 year-old female student with bilateral facial palsy (paralysis of 7th cranial nerve) as a result of Guillain-Barre Syndrome.
- FP was shown 42 slides of emotionally evocative and neutral stimuli (13 pleasant, 14 unpleasant, 15 neutral), and her emotional reaction self-rated on nine-point scale. Her scores did not differ from a normative sample of female students.
- In an emotional matching task, FP had to choose an emotional face from five to go with the emotion named, and the face to go with an emotional voice on audiotape. Her performance was "nearly flawless".
- In the emotion facial imagery test, she had to imagine an emotional face and answer questions about it (eg: "Are the eyebrows drawn together?"). Over 32 trials her accuracy was 97%.

Table 2.2 - Details of F.P (Keillor et al 2002).

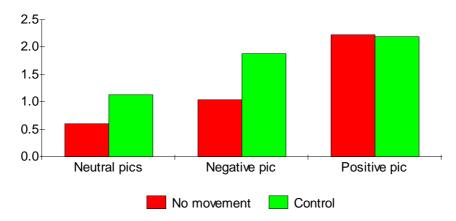
The "sufficiency hypothesis" version focuses upon facial expressive muscle activity as producing the emotional experience (eg: Ekman et al 1983). While the "modulation hypothesis" version views facial expression as modulating emotional experience. In this latter case, Strack et al (1988) found that participants asked to generate smile-related expressions reported more positive feelings than those asked to inhibit smile-related expressions in response to a stimulus. "In general, smiling makes a person feel more positive, and frowning makes a person feel more negative" (Davis et al 2009).

Asking participants to deliberately alter their facial expressions opens the possibility of demand characteristics as they are aware of the purpose of the experiment. Davis et al (2009) overcame this problem by placing dummy electrodes on the face ⁷ to measure brainwave activity. The participants were then told not to move their facial muscles to avoid "interference" ("no movement" group), which was really measuring facial expression inhibition.

One hundred and forty-two individuals from the "Columbia University community" in New York were shown four short video clips (one humorous, one fear-provoking, and two neutral). After each clip, participants rated themselves on certain measures, most of which were fillers, but emotional experience was the real focus.

⁷ "For the purposes of this study, it was important that the locations of the electrodes be over key muscle groups whose activity has been correlated with emotional experience... These muscle groups included the zygomatic muscles (smiling), the orbicularis oculi (laugh lines), the corrugator supercilii (frowning, furrowing the brow), and the frontalis (raising the brow)" (Davis et al 2009).

The "no movement" group reported significantly weaker emotional experience in response to the video clips than the control group (who were free to move their facial muscles) overall, but not for the humorous video clip (positive emotion) individually (figure 2.1).



(Source: Davis et al 2009)

Figure 2.1 - Mean self ratings of emotional experience (out of 8).

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3. ASSESSING ATYPICAL ANTI-PSYCHOTICS

- 3.1. Assessment criteria
- 3.2. Methodological issues
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3.1. ASSESSMENT CRITERIA

Atypical (or second-generation) anti-psychotics are a group of drugs developed in recent years, which, generally, have less (severe) side effects, and are more efficacious with (treatment-resistant) schizophrenia than conventional (or first-generation) anti-psychotics (Thomas and Lewis 1998) ⁸. Atypicals have a "broad efficacy spectrum" (Leucht et al 2009).

Atypical anti-psychotics are far more expensive than conventional anti-psychotics, so evaluation of them is crucial. Often studies use one global efficacy outcome, as do some meta-analyses (eg: Davis et al 2003) 9. A wider range of criteria includes:

- 1. Efficacy for total symptoms of schizophrenia eg: Song (1997) reported, from a meta-analysis of eleven randomised controlled trials ¹⁰, that risperidone was superior to a placebo, and at least equal to haloperidol (conventional anti-psychotic) in reducing a total symptom score on, for example, the Positive and Negative Syndrome Scale (PANSS) (Kay et al 1987). Leucht et al (2009) concluded, from their meta-analysis, that four atypicals (amisulpride, clozapine, olanzapine, and risperidone) were better than conventional anti-psychotics.
- 2. Efficacy for positive symptoms " of schizophrenia eg: sertindole (atypical) and haloperidol both superior to a placebo in a study with nearly 500 patients (Zimbroff et al 1997). Amisulpride, clozapine, olanzapine, and risperidone were superior than conventional anti-psychotics in the Leucht et al (2009) meta-analysis.

⁸ Technically, atypicals include older drugs, like thioridazine and sulpiride, as well as newer ones (eg: risperidone, clozapine) (Thomas and Lewis 1998). Leucht et al (2009) grouped nine drugs as second-generation - amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, risperidone, serindole, ziprasidone, and zotepine.

⁹ For example, the meta-analysis by Leucht et al (2009) used several outcome measures. The researchers searched for randomised controlled trials comparing atypical and conventional anti-psychotics, and 150 "good quality" studies were found.

¹⁰ Mattes (1997) has questioned the methodology of some of these trials.

¹¹ Eg: auditory hallucinations, delusions.

3. Efficacy for negative symptoms ¹² of schizophrenia - eg: Lieberman et al (1994) reported that negative symptoms responded to clozapine seven weeks after the positive symptoms had decreased. Leucht et al (2009) reported advantages with amisulpride, clozapine, olanzapine, and risperidone.

But there is discussion as to whether the negative symptoms are reduced (direct action) or that the improvement is due to less positive symptoms and reduced side effects. "Purists will say, probably correctly, that the case that any atypical improves primary negative symptoms has still not been made conclusively. Pragmatists will say, also correctly, that whether the negative symptoms which respond are primary or secondary is beside the point if the patient improves" (Thomas and Lewis 1998 p107).

- 4. Efficacy in treatment-resistant schizophrenia eg: clozapine has been reported as superior to conventional anti-psychotics like chlorpromazine with this group of individuals (Conley and Kelly 2001). But not all atypicals are better than conventional anti-psychotics here (eg: quetiapine, aripiprazole and paliperidone) (Melnik et al 2010).
- 5. Preventing relapse Leucht et al (2009) reported that olanzapine, risperidone, and sertindole were superior to conventional anti-psychotics here.
- 6. Improving neurocognitive deficits (eg: problems in perception, attention, and memory) It seems that atypicals are better for neurocognition than standard doses of conventional anti-psychotics, but this is "an accident" as atypicals "were not developed with neurocognition in mind" (Green 2002). However, it could be that the neurocognitive benefits are really the reduction in neurocognitive side effects (Green 2002).
- 7. Side effects This is viewed as the "undisputed advantage" of atypicals lack of extrapyramidal side effects (eg: parkinsonism, tics and facial grimaces) by all nine reviewed by Leucht et al (2009).

But other "milder" side effects, like weight gain, are more common (Schooler 2007). In fact, only aripiprazole and ziprasidone had significantly less weight gain than haloperidol (Leucht et al 2009). In the case of sedation, only aripiprazole less sedating than

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¹² Eg: catatonia, apathy.

haloperidol (Leucht et al 2009).

However, serious side effects (eg: agranulocytosis ¹³) are possible with clozapine, for example, though this appears to be related to having particular genes (Kelly et al 2007).

Less side effects lead to better adherence to treatment, and also improved quality of life.

- 8. Reducing unacceptable behaviour eg: clozapine reduces suicide risk, and physical aggression among patients with schizophrenia (Kelly et al 2007).
- 9. Efficacy in relation to co-morbid disorders eg: clozapine produces less substance abuse relapse among individuals with schizophrenia and substance abuse disorders (Brunette et al 2006). While five atypicals (eg: clozapine) were better than conventional antipsychotics for reducing depression (Leucht et al 2009).
- 10. Economic analysis Though atypicals are individually more expensive, their efficacy in reducing days in hospital, for example, can make them cost effective (eg: clozapine; Essock et al 2000).

3.2. METHODOLOGICAL ISSUES

There are many studies evaluating atypicals as compared to placebo and/or conventional anti-psychotics. For example, Schooler (2007) reviewed seventeen studies between 1975 and 2006 which evaluated anti-psychotics with first episode schizophrenia. But not all studies are comparable for a number of reasons:

- i) Length of study short-term (eg: 3 weeks) or long-term (eg: six months or more).
- ii) Administration of the drug oral or intra-muscular injection.
- iii) Outcome measure used eg: score on Brief Psychiatric Rating Scale (BPRS).
- iv) Whether participants are randomly allocated to the conditions.
- v) The use of blinding participants not aware if

¹³ This is a change in white blood cells, and occurs in about 1% of patients taking clozapine (Melnik et al 2010).

- receiving drug or placebo (single blind) and administrator of drugs not aware either (double blind).
- vi) Dose size eg: one study with risperidone used 3.3 mg/day while another gave participants 6.1 mg (Schooler 2007).
- vii) Fixed or flexible dose throughout study.
- viii) Definition of "clinical response" (ie: improvement) eg: $\geq 40\%$ improvement from baseline on BPRS in one study, while another used $\geq 50\%$ improvement (Schooler 2007).
- ix) Drug-naive patients or not.
- x) Sample size.
- xi) Drug and therapy combined or just drug treatment.
- xii) Definition of participant eg: "first-episode
 schizophrenia".
- xiii) Diagnosis of schizophrenia eg: DSM or ICD criteria.

Leucht et al (2009) concluded that atypicals (and conventional anti-psychotics) are not a homogeneous class, and so "improper generalisation creates confusion". Thus, some atypicals are better than some conventional anti-psychotics on some outcome measures.

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4. SOME ARGUMENTS FOR AND AGAINST DISTANCE THERAPY

With the development of modern communication technology in the 21st century has come therapy delivered via e-mail, video, instant messaging, telephone or texting, known as "distance therapy" (Epstein 2011) 14 15 . The big issue is the usefulness of distance therapy as compared to face-to-face therapy.

For example, early research (prior to 2003) found that clients reported satisfaction with videoconferencing techniques, and there was some evidence of its effectiveness with depression and anxiety, for example (Monnier et al 2003). Analysis of published studies between 2003 and 2008 supported these findings. Videoconferencing does not seem to alter the therapist-client relationship from face-to-face sessions. Clinical effectiveness has been shown mainly with case studies and a few controlled trials (Richardson et al 2009).

Barak et al (2008) examined the published research in English on the effectiveness of online therapy up to March 2006, and performed a meta-analysis on the 92 studies. This type of therapy was found to be as effective as face-to-face therapy, particularly for anxiety and stress.

Arguments For

- 1. Cheaper than face-to-face therapy. One advocate of etherapy in the USA pointed out that \$500 courses could be available for 25 cents (quoted in Nowak 2008).
- 2. No time wasting in sessions with "introductory chitchat" as in face-to-face interactions, straight to the point.
- 3. With e-mail and text therapists and clients can track thread of exchanges.
- 4. Therapist perceived as in the client's house via the computer.
- 5. Encourages honesty, and less fear about negative

¹⁴ A number of different terms have been used including online therapy, cybertherapy, Internet therapy, and e-therapy (Barak et al 2008). It could also include self-help website-based therapy, and virtual reality simulators.

¹⁵ A key difference between methods is whether the interaction is in "real time" (synchronously) (eg: videoconferencing) or delayed (asynchronously) (eg: e-mail).

facial reactions by therapist to information.

- 6. Easy to schedule, particularly for busy clients.
- 7. Protects client's privacy (eg: not seen going into therapist's office).
- 8. Less risk of physical and sexual abuse by therapist or client compared to face-to-face therapy.
- 9. No geographical boundaries, or issues of therapy not available in certain areas.
- 10. Overcomes shortage of trained therapists.
- 11. Texts and tweets can work as "boosters" to help clients in the daily struggle with addiction, for example.

Arguments Against

- 1. Some individuals benefit from the role expectations of the social situation of the therapist's office.
- 2. There is a loss of non-verbal cues in e-mail and text exchanges.
- 3. Physical contact (when appropriate) is not possible.
- 4. Some therapies involved complex interactions that are difficult and cumbersome when not face-to-face.
- 5. Skilled therapy is difficult to administer in short texts etc.
- 6. Assumes access to communication technology, and thereby discriminates against those without mobile phones, computers etc.
- 7. There is privacy in a therapist's office which may not be possible in the house of the client (eg: other people have access to therapeutic interaction).
- 8. Even admitting to family members about a problem and needing help may be an issue, and such individuals can go secretly to a therapist.
- 9. Concern over fraud when therapist and client never see each other. Abuse can still occur even though therapist and client never met.
- 10. The issue of unregulated e-therapists and sites. There is limited ability for official bodies to regulate

therapists who may be in another country.

11. Dealing with mental health emergencies that are many miles away.

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5. COMPASSION-FOCUSED THERAPY

Gilbert (2009) described compassion-focused therapy and compassionate mind training which focus on developing self-compassion among sufferers of mental disorders. It was observed that many sufferers have high levels of shame and self-criticism, and this limits their improvement in therapy.

The high level of self-criticism is seen as the basis of many mental disorders, and it is the maladaptation of the evolved "threat-detection and protection system". Early experiences of abuse, bullying, or neglect, for example, can make the individual oversensitive to threats of rejection from others which becomes self-criticism. This self-criticism is a "safety strategy", but it leaves the individual vulnerable to anxiety, depression, and low self-esteem.

The aim of compassion-focused therapy is to replace the automatic self-criticism with self-kindness, and to encourage the evolved "contentment system" to thrive. This involves compassionate mind training involving:

i) Attributes of compassion:

- Sensitivity.
- Sympathy.
- Care for well-being harness motivation to be caring.
- Distress tolerance.
- Self-empathy.
- Not being judgmental.

ii) Skills of compassion:

- Compassionate attention remembering examples when others were kind to us or we were kind to them.
- Compassionate reasoning finding alternatives to self-critical thinking.
- Compassionate imagery imagining exercises about the "ideal" of compassion (ie: what does it look like).
- Compassionate feeling experiencing compassion.
- Compassionate sensation exploring feelings in the body when being compassionate.

Gilbert (2009) noted a challenge of using compassion-focused therapy: "some clients have negative beliefs about compassion. Self-kindness too can be viewed with suspicion, as being soft, self-indulgent or not deserved. This usually indicates a fear of developing or experiencing self-compassion. Exploration might reveal that the individual is afraid that if they give up self-

criticism they will become lazy, unpleasant or unlovable. Some think that they will be punished for self-compassion by 'paying for it later' or having it taken away" (p206).

Gilbert (2009) presented compassion-focused therapy as adopting "the philosophy that our understanding of psychological and neurophysiological processes is developing at such a rapid pace that we are now moving beyond 'schools of psychotherapy' towards a more integrated, biopsychosocial science of psychotherapy" (p199). So it is a therapy that can be included with other types of therapy rather than as an alternative to them.

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