Commentary: Finding out the best way to tailor psychological interventions for children and families – a commentary on Ng and Weisz (2016)

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The article by Ng and Weisz (2016) on how to build a science of personalized intervention for youth mental health is ambitious and wide-ranging, being packed with penetrating analyses and imaginative proposals that set the agenda for psychotherapeutic research for years to come. It is driven by the desire to make therapy more effective, and underpinned by the notion that if therapy can be fitted more closely to individual characteristics, results will be better. This raises the question why sometimes therapy does not work, and brings its own headaches in finding suitable methods to get the answers.

Before we refine personalization: problems with existing service delivery
Before we get to the room at the top of the therapy house (it is on the second floor) to enjoy the beautiful view set out by Ng and Weisz (2016), we need to get past three elephants in the rooms on the ground floor. The first is the gross lack of availability of specialist services for the vast majority of the population with marked mental health problems. If we take a fairly high bar, those who have a diagnosis, who form around 10% of the population using conservative criteria, then only about a quarter receive any form of specialized treatment (ONS, 2005). In the United Kingdom, it is now government policy to make mental health have parity with physical health, but in practice this is a long way from what happens. The average expenditure is around £80 ($120) per head of population per year for child and adolescent mental health, of which at least half goes on inpatient care, leaving outpatient resources painfully thin. So perhaps we might add the need to test low-cost intervention such as internet-based therapies to the research agenda. There is a burgeoning literature on, and even if it only addresses, say, 20% of cases, that could be a huge burden of morbidity relieved. One challenge will be to find out which personal characteristics lead youth to be suitable for this approach.

The second elephant in the room is that when one examines the flowcharts for many RCTs, a high proportion of those requiring treatment don’t end up starting the trial. Often this is 50–80% of initially selected or referred cases, so that RCT findings may end up relating to a particularly motivated and compliant group. So a major agenda for personalization research should be to find out what would enable people who currently do not take part in treatment to engage with services. In routine clinical practice, as well as in trials, dropout rates (often defined as completing less than half of the planned therapy) are often 20–50%. Skilled clinicians will negotiate collaboratively with the youth and their family what they are up for, but along the way things can change. For example, some young people find it difficult to persist in the homework that CBT requires after the first 2 or 3 weeks, yet may be unwilling to say so and vote with their feet by dropping out. Perhaps for them, therapies that seem more naturally conversational, such as Interpersonal Therapy may suit such youth better, but we need trials of baseline characteristics to find out how best to determine this. And not every service will have therapists who can provide a range of evidence-based therapy for the same conditions, and once they have engaged with someone for assessment, the client may not wish to switch to another therapist. There are studies on barriers to treatment involvement, but we need more trials examining approaches that get an increased uptake of those seeking treatment, which may include Motivational Interviewing, home visiting, and Internet-based therapies. Universal screening with school based counseling services can also be a way to help young people engage.

But isn’t personalization happening already?
The third elephant in the room relates to current practice. One could argue that the main problem in child mental health is that clinicians are too personalized and eclectic, that they fail to use anything close to an empirically supported therapy (EST); rather, they do the kind of therapy they learnt when they were in training and apply this approach to a wide range of problems. Then even when they think they are using ESTs, many may go too far off-road in altering them, thus losing fidelity to the model. Meta-analyses confirm that reduced fidelity of implementation leads to smaller effect sizes (e.g., Lipsey, 2009). Of course, the principles of therapy need to be applied somewhat flexibly, so that perhaps a more useful term is skill than just fidelity in the sense of...
rigidly following chapters in a manual. A question deserving further research is when do alterations to treatments become helpful (when they get called adaptive) and when do they worsen the outlook (when they get called lack of fidelity to the model). A separate line of research would be to randomize people to more experienced and skilled therapists versus those with less skill, and see how this affected outcomes. All these points are not to disagree with anything that Ng and Weisz (2016) propose, but rather to suggest that more services need to implement more training and supervision to get their staff up to a level as a springboard from which the research agenda can be launched.

Moving up to the first floor, we have to fight our way through a crowd of rather peeved clinicians. They challenge the notion that their approach is not already personalized. They argue it is a caricature to say that the young person comes into the room and after a somewhat brief evaluation due to time constraints, gets a label and has something ‘done’ to them with insufficient recognition of their individual profile. The current model taught to most clinicians includes a thorough assessment that involves carefully eliciting the presenting concerns and reviewing other symptom domains, then writing a formulation on causes (sometimes including the four ‘P’ factors: Predisposing, Precipitating, Perpetuating, and Preventive) followed by a treatment plan, taking all this into account. Part of the assessment should include the young person’s strengths and the wider environment, including parenting, school and neighborhood influences. The treatment is then personalized according to the presenting problem and what the family are prepared to undertake. Within particular diagnoses, evidence-based interventions already vary according to personal characteristics: for example, many guidelines suggest that for mild ADHD, parent training is the first line treatment, whereas if it is more severe, medication should be offered (NICE, 2009). And if for example, there are side-effects from medication such as sleeplessness, there are guidelines for managing that too (NICE 2013). As therapy progresses, the assessment of what constitutes the main problem may change, and new barriers to progress may emerge – a depressed adolescent receiving CBT may reveal that their parent is emotionally abusive, so that more family work is added. Most clinicians think they are adapting therapy according to response.

Personalization according to biological characteristics
At last we emerge on the top floor, as the poet Henley put it,1 with our heads bloody but unbowed. Here, there are many good views, although some are partially obscured by obstacles. Space precludes commenting on all of the excellent proposals made by Ng and Weisz (2016), but a number will be addressed.

The notion of personalizing treatments according to biological characteristics, as seen in genotyping for some cancers in physical medicine, is still quite a way off in the mental domain, but we do have some reasonably solid evidence of gene–environment interactions contributing to causation. Thus, for example children with the allele coding for lower levels of the neurotransmitter monoamine oxidase (MAOA) are more likely to become antisocial when exposed to significant abuse (Ouellet-Morin et al., 2016); those who have alleles associated with lower brain activity of 5HTT transport are more likely to develop depression when maltreated (Uher & McGuffin, 2010). Studies are underway to look at the heritability of treatment response, and the, 5HTT neurotransmitter gene seemed to moderate response to CBT for childhood anxiety, but unfortunately a replication study failed to confirm this (Lester et al., 2016). The genetic news is not all gloom, because in the last few years the notion of differential susceptibility has been used to suggest that rather than genes only conferring increased risk under adverse circumstances, some may also confer better outcomes under more favorable circumstances. For example, the Leiden group have shown that the dopamine receptor gene, DRD4 7-repeat allele works this way, conferring worse outcomes with insensitive parenting, but better outcomes than average with more sensitive parenting (Bakermans-Kranenburg & van Ijzendoorn, 2011). Thus, there is an emerging literature suggesting that several genes may confer more resilience to adverse environments. However, short of genetic modification of children and young people presenting in distress, the implications for psychological therapies are as yet unclear. But even when these effects are confirmed and found to be significant, the trials will then be needed to see whether different treatment approaches are indicated, for example, whether the more susceptible can have shorter duration treatment, and so on. There is an increasing number of replicated neural correlates of childhood mental disorders and heterogeneity amongst these whereby some youth have the brain changes and others do not; again, whether this leads to a differential treatment response remains to be determined.

Personalization according to subtypes of symptoms and comorbid presentations
On the other hand, subtyping diagnostic categories by different phenomenology has led to demonstration of different responsiveness to treatment. Past research had indicated that callous unemotional traits often lead to less change during parent training for conduct disorder, which led to research groups trying to develop new treatments according to subtype (Dadds et al., 2014).

Traditional meta-analysis identifies subgroups that may respond better or worse to interventions
by lumping together all participants in trials and taking the group mean. Much greater power can be achieved if meta-analysis can be carried out at the personal level. A conventional approach is likely to be less powerful and miss important moderating effects as it can only detect effect moderation by trial-level summaries rather than individual-level variables. However, often within trials there is substantial variation and by combining them at an individual case level, there is much greater power to detect effect moderation. Application of this approach to 14 RCTs of the same parenting program (Incredible Years) found that a range of family characteristics such as low income, lone parent, teenage parent, being in an ethnic minority and parental depression, which are usually associated with poorer long-term prognosis for children with conduct problems, did not moderate a less favorable response to the parenting program. These are important findings, since they suggest this form of child therapy can potentially reduce social inequalities (Gardner et al., 2016).

Modular therapies to address multiple conditions are a great step forward, since comorbidity in referred cases tends to be the rule rather than the exception. As noted by Ng and Weisz, The MATCH manual to address comorbidities amongst children with anxiety, depression, trauma, or conduct problems has been shown to outperform standard monotherapy for the main condition and usual care.

Problems identifying active ingredients in therapy and treatment targets

The notion of identifying mediators as the ‘active ingredient’ of an intervention is an attractive one. However, as many authors have noted, most studies at present are inadequate in their measurement and methodology. Many look at mediators before and after a treatment program, but not at intermittent points during treatment. This can lead to erroneous conclusions. For example, using this approach in parent training, reduced criticism is often found to be a mediator. However, it could be that behavioral methods taught during the intervention reduce antisocial behavior, so that by the end parents are less annoyed as a by-product, rather than an active ingredient. Another issue is that the true mediator may not be measured, and so we need to be cautious before dropping elements of intervention programs because they do not appear to mediate.

How treatment works for particular individual cases is an intriguing but important question. It is surprising how overall, duration of therapy is often not much related to outcome, suggesting that some people may derive benefit from a few sessions, whereas others may take much longer, and perhaps make use of different aspects of the therapy. Measuring client characteristics before the start of therapy, and then carefully measuring possible mediators as therapy progresses will be important in answering this. We also need more trials based on personal preference, to see whether those who are offered a therapy that they find more palatable then do better. And this links back to the technical question of moderated mediation, where different clusters of characteristics may also predict response. Most publish trials on factors affecting response analyze them individually, and do not take them together. This is curious, since it is been recognized for over 50 years that the prognosis of child mental health conditions worsens exponentially with the increased number of risk factors (Rutter, 1987). It seems likely, therefore, that outcomes will be improved if treatments are personalized to address not just symptomatology but also underlying risk factors and processes: for example, harsh parenting and low self-esteem worsen prognosis for most conditions. Personalizing treatment to address these issues should help, along with promoting resilience.

However, whether we should go as far as suggested in proposal 4c by Ng and Weisz (2016) is more contentious. Shifting away from diagnoses to psychopathological processes risks throwing the proverbial baby out with the bathwater. Thus, for example, both depression and conduct problems can be associated with low self-esteem, and also poor emotional regulation, but addressing these two processes would not necessarily lead to improved outcome compared with current treatments, which actually are more personalized in the sense that they recognize the different presentations.

Conclusion

The annotation by Ng and Weisz (2016) offers a rich diet of theoretical processes and practical research designs to gain a deeper understanding of how best to personalize treatment. All the concerns raised above could be addressed by deploying the wide variety of strategies they propose, including sequential, multiple assignment trials to unpick what is working. Pleasingly, by no means do all of their proposals require a multimillion dollar research budget. Many relate to gathering data in everyday practice, analyzing it and then varying treatment accordingly. In the United Kingdom, the rolling out of routine outcome monitoring to the majority of services as part of the Children and Young People’s Increasing Access to Psychological Therapy initiative (visit www.england.nhs.uk/mentalhealth/cyp/) during therapy now offers an opportunity to get started down this road.

Acknowledgements

This commentary article was invited by the Annual Research Review Editor and has been subject to inter-
nal review. The author has no competing or potential conflicts of interest.

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Note
1. Henley wrote this poem after having one tuberculous leg amputated. Surgeons wanted to take off the other one, but believing in personalised medicine, Henley contacted the leading surgeon of the day, Lister, who managed to preserve it through repeated operations.

References

Accepted for publication: 3 February 2016