ADHD and the power of generalization

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DOI:
10.33612/diss.84379221

Chapter 2

ADHD and the power of generalizations

Based on:

Batstra, L., te Meerman, S., Conners, K., & Frances, A. (2017). Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults. The Lancet Psychiatry, 4(6), 439.

Abstract

This chapter discusses a meta-analysis of case-control studies into brain-anatomy of ADHD, comparing a group of people classified with ADHD to those without this classification. The findings indicated that -on average- 5 brain parts were smaller in children classified with ADHD. The effect sizes of the findings were minor, which means that in many with an ADHD classification those brain parts were larger than than in many without a classification. At the same time, in many without a classification thoser brain parts are smaller than in those classified with ADHD. Furthermore, the average differences disappeared in adulthood. Nevertheless, the authors erroneously concluded that their findings mean that ADHD is a brain disorder and that this message could be given to individuals with an ADHD classification. The authors were criticized for their faulty group-to-individual generalization. However, they did not change their conclusion when confronted with the criticism. In this chapter, the authors' response to the critique is analyzed.

Introduction

According to a paper by Hoogman and colleagues clinicians can now tell patients and their parents that children with ADHD "have altered brains; therefore ADHD is a disorder of the brain" (Hoogman et al., 2017b, p. 316). In this chapter, I will discuss our response to the Hoogman paper, the largest meta-study to date on brain anatomy and ADHD. The study compares the brain anatomy of 1713 individuals with an ADHD-classification to 1529 controls. In the general introduction of this thesis, I posited that generalizations are probably the most important mechanism behind inflated research findings and reification of ADHD. I view the widely publicized and cited Hoogman paper as the epitome of the power of generalization and this chapter is therefore a good starting point for this thesis.

Many others also had serious objections to the Hoogman paper, including several scholars. A petition to withdraw the study on blogsite "Mad in America" has been signed 1800+ times and continues to be discussed online. Both Allen Frances, who is the former chair of the DSM-IV taskforce, and Keith Conners, who is considered the founding father of the ADHD-concept co-authored our letter to the publishers. Throughout the years, both have continuously voiced concerns about the overdiagnosis of ADHD. In 2013 Keith Conners said about the rate (15%) of children classified as having ADHD: "The numbers make it look like an epidemic. Well, it's not. It's preposterous," (…) "This is a concoction to justify the giving out of medication at unprecedented and unjustifiable levels." (Schwarz, 2013).

During the submission of our reply, Keith Conners was very ill and he passed away some two months after publication. To our knowledge, the letter is his last scientific output. We have reprinted our response to the Hoogman study and will discuss the authors' reply to our criticism in detail. We will first demonstrate the logical flaws and the rhetorical devices they employ to deflect our arguments. Although we acknowledge the merits of the study, we criticize the authors for making far-reaching, misleading and harmful claims that are not supported by their data.

Reply to the Hoogman Study

The following is our full reply to the Hoogman paper:

> *"In their study on attention deficit hyperactivity disorder (ADHD) and brain volume, Martine Hoogman and colleagues concluded: "We confirm, with high-powered analysis, that patients with ADHD have altered brains; therefore ADHD is a disorder of the brain. This message is clear for clinicians to convey to parents and patients,*

which can help to reduce the stigma of ADHD and improve understanding of the disorder" (Hoogman et al., 2017b, p. 440). Such a definitive statement, however, is not supported by their data. In our view, their statement is wildly speculative and dangerously misleading at a time when ADHD is already overdiagnosed and overtreated with medication in high-income and middle-income countries (Merten, Cwik, Margraf, & Schneider, 2017).

In their well-executed study, Hoogman and colleagues reanalysed data from 23 sites for brain volume differences in children and adults diagnosed with ADHD. On the basis of Cohen's d values ranging from −0·19 to −0·10, the authors state that the volumes of the accumbens, amygdala, caudate, hippocampus, and putamen, and the intracranial volume, were smaller in individuals with ADHD than in healthy individuals. However, such small effect sizes mean that approximately 95% of the two groups overlap, and are usually interpreted as negligible or very small differences.

Even in studies with more compelling effect sizes than in this study, interpretation of differences between ADHD-diagnosed and ADHD-undiagnosed groups is complicated. Within-group variation is always large and between-group differences are small and do not apply to many individuals diagnosed with ADHD. Furthermore, associations do not necessarily imply causality. When Hoogman and colleagues wrote that their study proves that ADHD is not "caused by incompetent parenting", they do so without referring to the brain's plasticity and the fact that environmental factors can change brain anatomy. Additionally, the behaviour we call ADHD is not caused by either brain defect or bad parenting, but is associated with many different factors, ranging from poverty (Pastor, Reuben, Duran, & Hawkins, 2015) to pesticide exposure (Yu et al., 2016).

Biological differences do not automatically imply abnormality or pathology. According to Hoogman and colleagues, calling ADHD a brain disease can help to reduce the stigma of ADHD. This reduction of stigma does not, of course, justify labelling ADHD a brain disease if it is not, but more important, to label ADHD a brain disease is also simply wrong. Many people feel stigmatised and hopeless when told they have a brain disease (Reiner, 2011).

The fact that the message of this large-scale study now proving that ADHD is a brain disorder has already been widely echoed in the media is seriously concerning. This message risks misinforming the general public about the nature of ADHD, and could harm those diagnosed with the disorder. Furthermore, such simplification might easily increase the risk of sociological and other environmental factors related to (perceived) problematic behaviours being overlooked. Yet the most important

argument against the authors' conclusion that "patients with ADHD have altered brains" is that it is not supported by their own findings." (Batstra, te Meerman, Conners, & Frances, 2017, p. 439).

Reflection on author's reply

The journal published four critical reactions to the Hoogman study, including ours. Hoogman et al. addressed the criticisms in these four letters in one, also published, response. We include the third paragraph of their reply. In this paragraph the authors partly address our issues and those of Dehue and colleagues and we will analyze every statement of it. Additionally, we focus on several statements made later in the authors' reply in which they implicitly address other concerns we voiced.

"The critical letters by Dehue and colleagues and Batstra and colleagues claimed that we observed only small effect sizes and hence cannot conclude that individuals with ADHD have a brain disorder. ADHD is a disorder by all standards of psychiatric nosology, and our data support the idea that neuroanatomic brain abnormalities, although subtle, are associated with the disorder. The strength of our work comes from combining data collected worldwide. The observed brain abnormalities are heterogeneous and are likely to differ in individuals with ADHD (..). However, such heterogeneity at the individual level does not undermine the importance of effects at the group level. The criticisms of small effect sizes raised by these letters imply that we should only use the term brain disorder when everyone with the disorder shows the same pattern of brain abnormalities. By that definition, no psychiatric disorder would be a brain disorder. Our critics further ignore that our findings fit well with other features of ADHD, such as the link between emotional dysregulation and the amygdala, and the links between altered reward processing and striatum, to name just a few. Placing our findings within the broader scientific literature, as we did in our Article, provides the context for our conclusion." (Hoogman et al., 2017a, p. 440)

Avoiding and misrepresenting our criticism

The authors first summarize our response: "The critical letters by Dehue and colleagues and Batstra and colleagues claimed that we observed only small effect sizes and hence cannot conclude that individuals with ADHD have a brain disorder" (Hoogman et al., 2017a, p. 440). On the surface, this covers our criticism correctly, although we emphasized that the differences "do not apply to many individuals diagnosed with ADHD" (Batstra et al., 2017, p. 439). This is important, as this individualized message is exactly

what group data with small effect sizes cannot convey, which is the core of our criticism. The authors ignore this and focus attention on the ADHD construct: "ADHD is a disorder by all standards of psychiatric nosology". This is not something we questioned but is perhaps intended as a retort to Dehue and colleagues who –in line with Dehue's earlier work- (Dehue, 2014) forwarded that people, and not brain scans can decide on what is a disorder (Dehue et al., 2017, p. 438). Although there is overlap between our response and that of Dehue et al., we did not raise this fundamental issue and we will not reflect on it here.

The authors add: "and our data support the idea that neuroanatomic brain abnormalities, although subtle, are associated with the disorder" (Hoogman et al., 2017a, p. 440). We have not denied this and the statement is not untrue, however a (weak) association means that such brain "abnormalities" –or 'differences' as we prefer to call them- are far from unique to the ADHD group: they are not necessary nor sufficient for displaying such behaviors. Social adversity, such as lone parenthood and poverty are also –and more strongly- associated with ADHD-behaviors (Hjern, Weitoft, & Lindblad, 2010; Russell, Ford, Rosenberg, & Kelly, 2013), yet of course clinicians do not tell all those classified with ADHD and their parents that they are poor or divorced. The authors ignore the issue and continue with: "The strength of our work comes from combining data collected world wide" (Hoogman et al., 2017a, p. 440). This is a tenuous effort and one of the reasons we have praised them for their study, but it is not relevant to our criticism.

Then, the authors follow this up with a very relevant inaccuracy: "The observed brain abnormalities are heterogeneous and are likely to differ in individuals with ADHD" (Hoogman et al., 2017a). At first glance, this may seem to address our issue of heterogeneity in the research groups, but in fact it does not. Tindale calls such a strategy a "fallacy of diversion" (Tindale, 2007, p. 19) as it diverts attention from the issue we really address. In particular, this type of diversion is called a "Straw man", which means a similar, but in fact different, argument is contested (Tait, 2009, p. 247). We posited that brain sizes in those with an ADHD classification differ, and –with low effect sizes- group differences do not apply to many with or without an ADHD classification. The authors avoid this issue and suggest that all those with ADHD have at least some type of abnormality while their data do not show this. On the contrary, many people in the ADHD group do not have any of the alleged brain "abnormalities", while in the control group almost as many have these variations. In society at large, these variations are even expected to be far more common in "normal" people than in the ADHD-group.

Then the authors add: "However, such heterogeneity at the individual level does not undermine the importance of effects at the group level". This, again, is a diversion -another straw man- as it turns our argument around. We, nor Dehue et al. (2017), have stated that the individual heterogeneity undermines the importance of effects at the group level. We stated the opposite, that group level findings give little bearing for what we tell individuals and therefore contested their take home message that clinicians can tell all ADHD diagnosed individuals they have a disorder of the brain.

The authors continue with their false suggestion that those with an ADHD classification have at least one abnormality: "The criticisms of small effect sizes raised by these letters imply that we should only use the term brain disorder when everyone with the disorder shows the same pattern of brain abnormalities". We have not suggested nor implied the same pattern of brain abnormalities is a precondition for such a claim. However, if clinicians are told they can tell individual patients and parents that they have a disorder of the brain, we should at least be certain that those individuals have at least one outstanding difference from a typical brain. This is not what their own data show. Smaller brains are –again- not necessary or sufficient for an ADHD diagnosis, and similar "abnormalities" –by whatever standard- occur in those without an ADHD classification.

"Others are doing it too": Ad-populum and authority appeals

The authors then state: "By that definition, no psychiatric disorder would be a brain disorder". However, we are discussing the authors' conclusions and the empirical evidence in relation to ADHD and not other classifications of disorder. First, this seems to be a typical "Ad-Populum Fallacy". Although it might be a popular habit to interpret brain associations as valid for concluding behavioral classifications are brain disorders, "truth is not simply a popularity poll" (Tait, 2009, p. 247). What other authors conclude about other psychiatric disorders and on what basis is not at stake. Second, if they would like to make comparisons to other psychiatric disorders, the taskforce of the DSM-5 unequivocally stated: "it can be concluded that the field of psychiatry has thus far failed to identify a single neurobiological phenotypic marker or gene" (Kupfer, First, & Regier, 2002) and "not one laboratory marker has been found to be specific in identifying any of the DSM-defined syndromes" (Ibid, p. xviii). Blogsite Mad in America candidly retorted that with this, "Hoogman and colleagues themselves sum up the arguments of their critics nicely" (Simons, 2017). Indeed, there are no abnormalities unique –by whatever unclear standards a difference can be considered an abnormality- for those classified as having ADHD or any of the other DSM disorders.

The merits of the study

Next, the authors comment: "Our critics further ignore that our findings fit well with other features of ADHD, such as the link between emotional dysregulation and the amygdala, and the links between altered reward processing and striatum, to name just a few" (Hoogman et al., 2017a, p. 440). We have not "ignored" those associations, but simply considered it irrelevant to the issue of unjust generalizations of small group findings to individuals we addressed. However, in case the authors feel we have insufficiently acknowledged the value of their work, we do acknowledge that their study could indicate that the behavior of some individuals who are classified with ADHD could be related to maturational differences of brain parts associated with emotion regulation such as the amygdala. However, there are other theoretical possibilities as well: neuroplasticity, often seen in musicians (Hyde et al., 2009), indicates possible environmental influences on brain growth. Furthermore, prenatal alcohol exposure is also associated with inhibited brain growth (Archibald et al., 2001). This raises an important conceptual issue: should we include those prenatally exposed to alcohol when studying the brains of those classified with ADHD? Or should we in fact consider this a confounder that creates an artefact in group studies such as by Hoogman and colleagues? In other words, are we not diagnosing the wrong disorder in some cases and erroneously including those with affected brains due to prenatal exposure ADHD brain studies? For a discussion see for instance (Kable et al., 2016; Peadon & Elliott, 2010).

The authors end the third paragraph with: "Placing our findings within the broader scientific literature, as we did in our article, provides the context for our conclusion" (Hoogman et al., 2017a, p. 440). However, the broader scientific literature shows many statistical associations between ADHD behaviors and for instance divorce, poverty, parenting styles, lack of sleep, abuse, and much more (Richards, 2013; Russell, Ford, Rosenberg, & Kelly, 2013; te Meerman, Batstra, Grietens, & Frances, 2017; Thapar, Cooper, Eyre, & Langley, 2013). Hence, while we do acknowledge brain maturation is associated with the ADHD construct, we feel that the broader scientific context provides no empirical ground whatsoever for dichotomizing the discussion by concluding that ADHD is a disorder of the brain.

Correlation and cause

In the fifth paragraph, the authors address our concerns about confusing correlation and causality. They write: "Although concluding that ADHD is a brain disorder, we did not claim that the neuroanatomic changes reported were causal. The cause of ADHD is complex, and genetic and environmental factors and their interplay will affect brain

structure and function, which in turn will mediate effects on the clinical phenotype. As suggested, chronic altered patterns of behavior, such as persistent inattentiveness and hyperactivity impulsivity [sic], might also influence brain structure and function". The authors acknowledge at least some of the etiological complexity of these behaviors. And indeed, the authors have not explicitly claimed causality. However, we fear that just as influenza is called a viral infection, addressing the cause, the label "brain disorder" might be interpreted as implying causality. And again, as brain size is a mere weakly associated factor among many others, this is still a misleading suggestion just as a statement like "ADHD is a poverty disorder" would be.

Waiving responsibility

The authors end their paragraph as follows: "Finally, we cannot address concerns about press coverage; we discuss only the science reported in the paper and provide further rationale for our conclusions" (Hoogman et al., 2017a, p. 440). By this the authors evade responsibility for the fact that they generalized the group findings and also added this label of a "brain disorder" to their press release as Dehue et al., (2017) rightly assert. Furthermore, the main author emphasized the message that ADHD is just a brain disorder and not related to, for instance, bad parenting- in an interview (Waterval, 2017). We fear that with this simplistic notion the authors facilitate others to overlook complex societal problems such as poverty, flaws in the educational system, divorce, intra-familial violence, and social exclusion.

In the final paragraph, the authors also address the subject of stigma we brought up. "We wrote that understanding ADHD as a brain disorder might help reduce stigma, rather than increase it, a view shared by many others, including the US National Institute of Mental Health and patient and service user advocacy groups". The authors give no other argumentation than an ad-populum argument (Tait, 2009): "a view shared by many others" and an appeal to authority (Ruscio, 2006). In so far as one might indeed acknowledge that a mental health institute should have some authority in such matters, it must also be noted the NIMH does not have a particularly strong reputation as the US is often considered the "epicentre of the 'ADHD diagnosis'" (Erlandsson, Lundin, & Punzi, 2016, p. 3). The lack of control in the country with regard to market influences in healthcare, for instance by allowing direct to consumer advertising (Donohue, Cevasco, & Rosenthal, 2007), is notorious.

More importantly, it is unclear on which sources the authors base their claims about the presumed attitude of the NIMH. Hopefully, both the authors and the NIMH ac-

knowledge the wider scientific context that stresses the far from dichotomous relation between neuro-reductionism and stigma. There is empirical proof for bio-reductionistic explanations being a "mixed-blessing". While they tend to alleviate guilt for problematic behaviour by suggesting lack of personal influence and responsibility, bio-reductionistic explanations are likely to stigmatize in other areas. For instance, a meta-study of experimental research suggests bio-reductionistic explanations increase perceived dangerousness and prognostic pessimism (Kvaale, Gottdiener, & Haslam, 2013). A meta-study of correlational research found an additional likeliness for increased social distance (Kvaale, Haslam, & Gottdiener, 2013). For a recent meta-study, see Loughman & Haslam (2018).

The end justifies the means?

Finally, the authors seem to suggest that the end justifies the means: "We recognise that some disagree. However, we have no doubt that we all share the desire not to return to the relatively recent days when individuals with ADHD were dismissed as lazy, having bad parents, or being bad children. Understanding of ADHD as a brain disorder and clarifying the extent of its biological origins has helped direct focus away from moral judgments towards developing evidence-based treatment of the impairing symptoms of this disorder". Of course, it is wrong to label children or their parents as being bad without knowing the reasons for the child's behavior. However, as these ADHD-related behaviors are associated with many factors of which brain maturity is only one, the authors have simply jumped from one simplistic generalizing notion to another by suggesting these behaviors are caused by a brain disorder. Although this could theoretically explain attention problems and unruly behavior for a very small subgroup, it is simply wrong to tell this to individual children based on group data with small effect sizes.

Discussion

The suggestion that all those with an ADHD classification have "altered brains" as Hoogman et al. state, reifies ADHD and may lead to stigma. As the brain scans merely indicate very small group differences, the label of a brain disorder is likely to be misapplied to many classified with ADHD. Although we and other authors have voiced concerns, the authors hardly acknowledge the critique. Their reply – like their original paper- contains several fallacies and additional rhetoric devices that deflect our arguments and those of other authors.

It starts by avoiding the fact that group data are not applicable to many individuals with an ADHD classification, although the authors suggest they address this issue. However, the authors in fact only state that brain abnormalities differ across individuals diagnosed with ADHD, suggesting that all with an ADHD classification have at least some abnormalities. They conveniently avoid that such "abnormalities" occur almost just as often in the control group, and that far from everyone classified with ADHD has those alleged abnormalities. They then turn our argument around: they suggest we problematize the group level findings itself while in fact we problematize group level findings being applied to individuals.

The authors seem well aware that their generalizing conclusion, that all those with a classification have at least some kind of abnormality, is flawed. After avoiding this and reframing our objections, they continue with a mixture of ad-populum arguments and appeal to authority: some other psychiatric disorders with similar statistical associations relating to the brain are also called brain disorders and others, such as the NIMH, share their view on stigma.

The Hoogman study has received severe criticism by the Blogsite Mad in America, and more can be said about the article. For instance, an important point that has not been discussed in relation to this paper –to our knowledge- is the use of refined phenotypes and normal controls, a common practice that results in sample bias and places an extra burden on generalizing the findings and applying them on an individual level. Furthermore, theoretically it is even possible that most children with an ADHD classification have bigger brains than those without, despite the fact that –on average- research and control groups might show on average 'normals' have bigger brains. Such counterintuitive relations between group versus individual findings are studied by the ergodic theorem. Researchers from this school warn for the limitations of group studies and state that "we may need to reconsider how we communicate statistical principles to students and researchers" in relation to such studies (Fisher, Medaglia, & Jeronimus, 2018, p. E6107).

However, we do feel that the study also has merits. It is a very large study and collecting and analyzing so much data is an admirable scientific effort. And, as the authors address in their reply, the statistical associations of the delayed growth of, for instance, the amygdala could be relevant. Indeed, for some with an ADHD classification, a maturational lag might partly explain their propensity to have a different emotional response than others.

Nevertheless, rather than suggesting these people have a brain disorder, this could also lead to a conclusion that is far more respectful to the individual. Given that children

differ in their physical and psychological development, we could and perhaps should call into question society's problems to accommodate to children's idiosyncratic developmental pathways.