Chapter 5

Citation distortions in the literature on the serotonin-transporter-linked polymorphism and amygdala activation

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Abstract

Selective citation may contribute to the persistence of strong beliefs in research findings for which the strength of evidence is questionable or declining. For the literature on the putative association between the serotonin transporter polymorphism (5-HTTLPR) and amygdala activation, differences between citation rates for positive and negative studies are obscured by large differences within the negative group: whereas studies that claim to have found an effect (in spite of negative findings indicated by a standardized meta-analytic approach) are cited as much as positive studies, studies that neither report nor claim the existence of an effect (i.e., "refutation" studies) are typically overlooked. Moreover, the majority of recent studies ignore the methodological issues raised by a meta-analysis and only mention the presence of a significant meta-analytic effect. Researchers should focus on the nuance and caveats of previous work in their articles and be encouraged to publish and cite refutation studies.

Short report

A seminal finding in imaging genetics is that carriers of the short (S) allele of the serotonin-transporter-linked polymorphic region (5-HTTLPR) exhibit an increased amygdala response to negative emotional stimuli [295]. The original article by Hariri and colleagues has been cited over 1,000 times since its publication in 2002.

Although meta-analyses have shown a statistically significant (but small) effect across published studies, the validity of these findings is undermined by the presence of publication bias [296, 297]. Moreover, the strength of evidence has declined over time [298, 297]. However, the strength of belief does not seem to have decreased comparably. For instance, a recent review maintained that up to 5% of differences in amygdala activation can be explained by variation in the 5-HTTLPR [299].

One factor that may contribute to the persistence of belief in an effect is preferential citation of positive studies [44]. For the network of studies reported in the most recent meta-analysis on 5-HTTLPR and amygdala activation [297], citation differences between positive (n = 10) and negative studies (n = 15), although present, are not very pronounced. While 40% of studies are positive, they receive 55% of within-network citations and 67% of citations via Web of Science (49% excluding Hariri and colleagues, 2002 [295]). A positive study is cited, on average, by 39% (SD = 32%) of subsequent studies in the network, and negative studies are cited by 25% (SD = 24%). In Web of Science, average yearly citation rates for negative and positive studies are 11 (SD = 11) and 24 (SD = 32) times, respectively, with the latter declining to 15 (SD = 17) times when Hariri and colleagues (2002) [295] is excluded.

However, citation rates of negative studies can be confounded by studies with inflated claims or "spin" in their abstracts. Spin is the (intentional or unintentional) use of reporting strategies to emphasize the presence of an effect, for instance by focusing on statistically significant findings from subgroup analyses or secondary outcomes [178].

It was previously shown that many of the studies in Murphy et al. (2013) [297] make stronger claims in their abstracts than is warranted by the reported data when a standardized analytical approach is employed [300]. Figures 5.1 and 5.2 illustrate that "claim" studies – that is, negative studies that claim to have found an effect, but for which a standardized analysis does not indicate statistically significance evidence - are cited comparably to positive studies.

In contrast, studies that neither report nor claim the existence of an effect (i.e., "refutation" studies) are overlooked. Refutation studies, for instance, are cited by only 14% of subsequent studies within the network (figure 5.2, left panel) and they receive only 4% of citations in Web of Science (Figure 5.1, right panel). Refutation studies appear to face a double difficulty in contributing to and changing the common perspective: not only is it hard to publish them, but they are also cited infrequently once published. Studies are

rewarded for making positive claims by higher citation rates, resulting in a literature that presents a distorted impression of the strength of evidence.

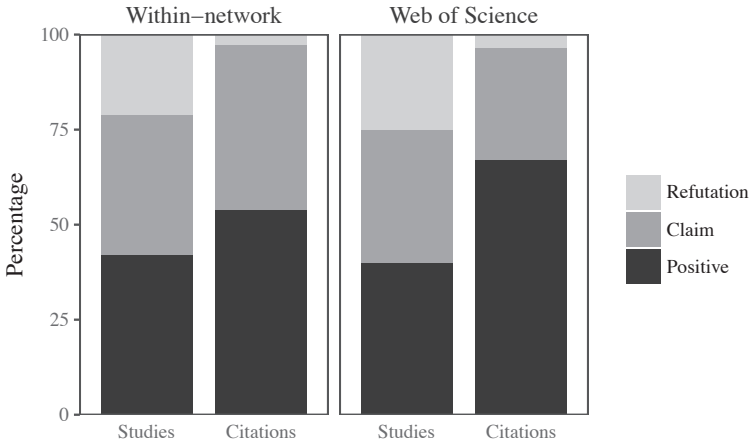

Figure 5.1: *Percentage of studies of each type (positive, claim, and refutation) and the percentage of citations received by each type of study for within-network citations and Web of Science citations. For within-network citations, the final study within the network was not included in the number of studies, as it could not have been cited within the network.*

Effect estimates by meta-analyses are not affected by spin and often swiftly become the new standard in the field. Although meta-analyses can potentially override the effects of citation distortion, they can also lead to further distortion when important issues they raise are neglected. Two independent raters coded whether the 37 peer-reviewed English-language articles citing Murphy et al. [297] (source: Google Scholar, November 2014) referred to these authors' concerns about issues of statistical power and publication bias, or only mentioned the presence of a statistically significant effect.

Three methodological articles did not address the outcome of the meta-analysis, and one did not provide enough information for coding. Of the remaining 33 articles, only seven reported Murphy et al.'s concerns, and one article discussed similar issues more broadly. In other words, 76% of recent studies cite the meta-analysis as evidence for the association without expressing concern regarding the validity of this conclusion.

Who and what is cited colors the common perception of an evidence base. For the association of 5-HTTLPR genotype with amygdala activation, we have shown that refutation studies are typically ignored and methodological concerns reported by a meta-analysis are often overlooked. Researchers should focus on the nuance and caveats associated with any result (including those derived from a meta-analysis) in their articles, and should be encouraged to publish and cite refutation studies. A recent study published individual (null) results together with an updated meta-analysis, an approach that might help increase the visibility of refutation studies [298]. Citation analysis of other topics could

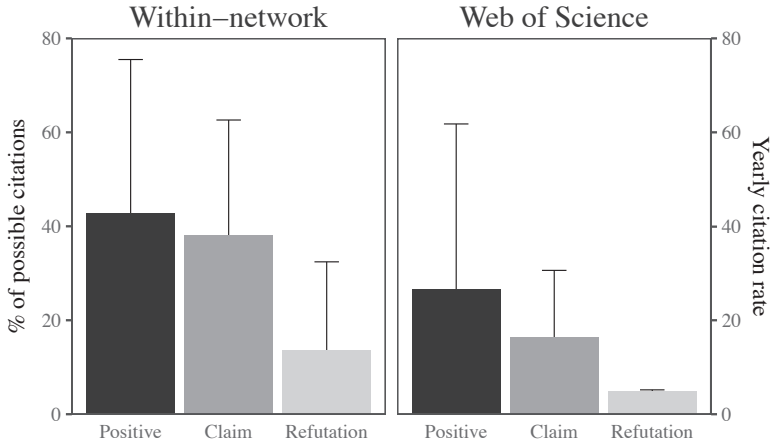

Figure 5.2: *% of possible within-network citations (±1 SD) and yearly Web of Science citation rate (±1 SD) for positive, claim, and refutation studies.*

help clarify why certain beliefs remain deeply rooted in the field and support researchers in distinguishing fad from fact.