Addressing Suggestibility as a Psychological Phenomenon in Clinical Trials

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Introduction

Modern clinical trials increasingly rely on technologies to help accelerate startup, capture endpoints, and facilitate recruitment. In the midst of this technological revolution, it becomes increasingly important to understand patient perspectives and to anticipate how subjects in research studies may be impacted by the presence of digital tools, devices, and mobile health applications in clinical research.

One area that deserves further exploration is how technologies impact participant beliefs in clinical trials and whether this may alter responses to treatment by modulating suggestibility.

Suggestibility as a Psychological Phenomenon. Suggestion can contribute to the uncritical and/or unreasoned responses to a situation (Coffins, 1941). Suggestions can be classified into two types: direct and indirect. Indirect suggestions occur when the implication is hidden, while direct suggestions occur when the prompting is not concealed (Polczyk, 2016). Within these two types, there are three primary areas of suggestibility that have been studied and researched extensively: the placebo effect, hypnotic suggestibility, and interrogative suggestibility (Halligan & Oakley, 2014). The placebo effect is the effect of a medication or course of action that cannot be accredited in any way to the actual treatment (Halligan & Oakley, 2014). Hypnotic suggestibility is the degree to which people respond to suggestions while under the influence of hypnosis (Halligan & Oakley, 2014). Interrogative suggestibility is how much a person will give in to a suggestive question and how much that person will change his/her answers after the person in control exerts pressure on him or her (Gudjonsson, 1894). Placebo effect and interrogative suggestibility are considered indirect suggestions while hypnotic suggestibility is categorized as a direct suggestion.

Placebo Effect:

Suggestibility is a relevant and prominent issue in clinical trials today. It has the power to distort people's perception of the world around them in order to align with their conscious or unconscious expectations (Varelmann, Pancaro, Cappiello, & Camann, 2010). Suggestibility has caused patients to experience higher levels of pain compared to a counterpart group which received the same treatment without suggestions (Varelmann et al., 2010). The placebo effect has led control group subjects to report symptoms directly related to the ones mentioned in the informed consent form (Kaptchuk et al., 2006). Some subjects in that placebo group even dropped out of the study because they experienced such severe side effects. (Kaptchuk et al., 2006). Although these instances showcase the negative effects of suggestion, there have also been various positive outcomes associated with

suggestion. For example, research has shown that a doctor's use of suggestion during drug interviews positively impacts the recovery status of patients diagnosed with conversion disorder. (Poole, Würz, & Agrawal, 2010). Although suggestibility in clinical trials can have positive effects, its most relevant and concerning impact is the placebo effect.

Hypnotic Suggestibility:

Suggestibility in clinical trials has been shown to be connected to hypnotic suggestibility (Sheiner, Lifshitz, & Raz, 2015; Barber, 1965). Researchers found that one's level of hypnotic suggestibility is related to how much placebo effect one will experience during an experiment (Sheiner et al., 2015). More specifically, placebo effect and hypnotic suggestibility have a similar underlying factor: response expectancy. Response expectancy is the expectation of an automatic and subconscious reaction in response to a cue (Kirsch, 1999). When participants received suggestions from the researchers or were given the unbiased instructions and then placed under hypnosis similar effects were produced (Barber, 1965). In other words, post-hypnosis task performance is shown to be similar to post-suggestion task performance. The results of these studies support the theory that suggestibility in clinical trials and hypnotic suggestibility are related.

Interrogative Suggestibility:

Suggestibility is not only found in the clinical and research environment but also in other fields. In the criminal justice system, when suspects are being questioned there is the concern that interrogative suggestibility may occur. Interrogative suggestibility, as stated earlier, is how likely someone is to be persuaded to modify his/her beliefs and behaviors by misleading questions and badgering or coercive statements (Halligan & Oakley, 2014; Gudjonsson, 1894). It is possible for people to create faulty memories or even give false confessions because they were "suggested" to do so (Gudjonsson, 1984). This is different from other types of suggestibility because it involves a closed social situation with one person in control, a leading method of questioning and a required behavioral response (Gudjonsson, 1987). This type of suggestibility showcases how research on this subject may lead to positive outcomes for those in the criminal justice system as well as participants in clinical trials.

Solution/Conclusion

Suggestibility is a variable that researchers have the potential to address and manage, through introspection and planning. Results suggest that internal factors such as self-judgement, and external factors, for example, the amount of information given and the interviewer's demeanor, can contribute to a person's level of suggestibility (Bain, Baxter, & Fellowes, 2004). Participants with lower self-esteem were more likely to change their answers after being pressured to do so. Whether subjects had a friendly interviewer or were warned of the presence of deceptive information, the occurrence of either of these conditions resulted in subjects being less likely to give in to misleading questions and less likely to be suggestible over all (Bain et al., 2004). To solve the issue of suggestibility in clinical trials, researchers must first try to identify participants' overall level of suggestibility and then focus on the minimization of this characteristic. In order to identify and decrease a person's level of suggestibility, the cause(s) of said suggestibility must be identified.

It is generally agreed upon that there are three factors which can influence suggestibility: situational factors, usual and/or current states, and personality traits (McDougall, 2000; Gheorghiu, Netter, Eysenck, & Rosenthal, 1989). There is also a fourth factor that has been acknowledged but not as widely discussed by researchers: a lack of knowledge and/or flawed organization surrounding the subject matter being conveyed (McDougall, 2000). Situational factors include elements such as a prestigious and accomplished person communicating the suggestion, group pressure, and placebo response. Usual and/or ongoing states include motivation/attention, expectations, and atypical brain conditions (hypnosis). Personality traits are the individual characteristics of the person receiving the suggestion, including their disposition to delusion and degree of conformity (McDougall, 2000; Gheorghiu et al., 1989).

Excepting a subject's individual characteristics, researchers have the power to modify the conditions that influence suggestibility. If a potential subject is labeled as suggestible, researchers should ensure that a 'neutral person' is interacting with the participant and providing the subject with the best and most well-organized information. Technology can help solve the problem of how to present organized and clear information to patients. According to a survey given to participants, patients have stated that using healthcare technology improved their engagement and compliance during clinical trials (Henderson, 2015). Technology has been shown to have a significant effect on how participants understand the informed consent form, which is one of the main points at which participants' misunderstandings can turn into suggestions regarding the study's objective and possible side effects. A review and meta-analysis of studies comparing multimedia-based informed consent forms and a control condition, usually paper form, revealed a little less than one third of participants had a significant improvement in the level of understanding when using the technology-based form (Nishimura et al., 2013). A few studies

have found no significant differences between using an electronic versus paper informed consent or questionnaire, but many others clearly illustrate the positive impact of technology on patients' beliefs (Velikova et al., 1999; Varnhagen et al., 2015).

Using an electronic informed consent form compared to a paper form resulted in participants having a better understanding of the purpose of the research study. It also prompted participants to be more aware of other available options if choosing not to participate, and to remember more clearly whom they should contact with questions or concerns about the research (Rowbotham, Astin, Greene, & Cummings, 2013). Providing participants with an interactive computer-based presentation that delineates all aspects of the study and encourages participants to discuss risks/benefits with the doctor lead to patients being much more likely to understand the objective of an early-phase trial and much less likely to believe they would be cured by enrolling the research study, compared to the patients who received a paper pamphlet with the same information (Kass et al., 2009).

Not only does technology help with comprehension, it also increases patient participation rate. Presenting an informational video in addition to the informed consent, compared to just providing the written form, resulted in patients being more willing to participate in the research study, and in participants retaining more knowledge about the study when questioned a month later (Weston, Hannah, & Downes, 1997). Clearly, using technology to present information to participants has a positive impact on their level of understating of the study. This is important because it allows researchers to limit the ambiguity that arises when information is not presented clearly. Eliminating confusion and ambiguity through technology is done in the hopes of adjusting subjects' expectations/beliefs and decreasing the potential placebo effect. If suggestibility is not as flexible as proposed, then using a subject's level of suggestibility as a criterion for inclusion or exclusion from a study is advised.

To further explore the influence of technology on suggestibility, the current research needs to shift in two ways. First, future studies must move their main focus from how the presentation of information through technology influences participants' level of overall comprehension to how it influences participants' level of suggestibility. Secondly, research exploring how situational factors like computer-based treatments or digital measurement methods compare to their non-digital equivalents, and then how that in turn effects their influence on suggestibility, should be explored.

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