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Perspective

From information to follow-up: Ethical recommendations to facilitate the disclosure of amyloid PET scan results in a research setting

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Abstract In the field of Alzheimer's disease research, the use of biomarkers such as amyloid positron emission tomography (PET) has become widespread over a relatively brief period of time. There is an increasing tendency in research studies and trials to switch from no disclosure under any condition toward a qualified disclosure of individual research results, such as amyloid PET scan results. This perspective article aims to evaluate the possible need for a modification of the available recommendations on amyloid PET scan disclosure, based on recent empirical evidence obtained within the field of amyloid PET. This article also applies the International Guideline for Good Clinical Practice to the field of amyloid PET disclosure. Hence, we propose several recommendations to facilitate amyloid PET disclosure while minimizing possible risks of amyloid disclosure in a research context.

Keywords: Amyloid PET scan; Disclosure; Alzheimer's disease; Recommendations; Amyloid imaging; Disclosing information; Ethics

1. Background

There is currently no obligation for the researcher to disclose individual research results (IRRs) to the research participant. No one favors full disclosure under all circumstances or no disclosure under any condition [1]. In the field of Alzheimer's disease (AD) research, the use of biomarkers such as amyloid positron emission tomography (PET) has become widespread over a relatively brief period of time. There is an increasing tendency to switch from no disclosure under any condition toward a qualified disclosure of IRRs. This switch has been guided partly by the Appropriate Use Criteria of Amyloid Imaging and the Health Authorities approval of amyloid PET imaging in patients with a clinically defined memory impairment [2–7]. Grill et al showed how disclosure of amyloid status is not a barrier to the recruitment of participants in clinical trials [8]. A qualified disclosure policy implies that disclosure may take place if the result is in line with particular criteria. These criteria take into account the proof of clinical utility of the result and the actionability of the result (possibility to provide a treatment, symptomatic relief, etc.) [1,9]. Disclosure of results will also vary depending on three other factors: The first factor concerns the issue of active versus passive disclosure. Passive disclosure only takes places after explicit request of the research participant, whereas an active disclosure refers to a process whereby researchers

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actively offer results to the participant [1]. The second factor concerns the result itself: there is a difference between disclosing an aggregate group result, an incidental finding, or an individual research result [1]. The content of the data also makes a difference, for example, a standard blood value results or disclosure of a genetic risk factor. The third factor concerns the study population: There is a fundamental difference between disclosing information to cognitively healthy participants, participants who have a cognitive deficit, or participants who are already in a more severe stage of AD.

To our knowledge, four studies have developed recommendations about the disclosure of amyloid PET results. The recommendations from Porteri et al, Lingler et al, and Grill et al focus on mild cognitive impairment (MCI) patients, whereas the recommendations by Harkins et al targeted the disclosure of results to cognitively normal adults [10–13]. Three of four recommendations [10,11,13] focused on the disclosure of amyloid PET results, whereas one recommendation [12] pertains to biomarker-based information more generally. Relatively few empirical studies have explored the viewpoints of patients, carers, and stakeholders regarding amyloid PET disclosure [14–17].

This article aims to evaluate the possible need for a modification of the previously mentioned available recommendations [10,12], based on recent empirical evidence and the perspective of patients themselves [14,15,18]. This perspective article applies the International Guideline for Good Clinical Practice to the field of amyloid PET disclosure in a research context taking into account recent empirical evidence obtained within the field of amyloid PET. The review also takes into account relevant elements that have arisen from recent empirical studies of genetic AD risk disclosure [19]. We propose several recommendations to facilitate amyloid PET disclosure while minimizing possible risks of amyloid disclosure in the research context. Although this article focuses on the use of amyloid PET scans in research, the criteria set forward in this article may also be of interest for clinicians when using amyloid PET scans as part of the clinical diagnostic evaluation of their patients with cognitive problems.

2. From information to follow-up

Disclosure of results is associated with multiple ethical challenges. Based on the article of Porteri et al [12] that describes multiple important aspects of the informed consent process, we suggest a six-step recommendation to facilitate disclosure and to minimize possible risks of amyloid PET disclosure. This recommendation results in six concrete steps: Information (I), Decision (D), Testing (T), Confirmation (C), Return of result (R), and Postguidance (P). These are abbreviated as the IDT CRP recommendations (Fig. 1).

2.1. Information

Before testing, it is of key importance to provide accurate, clear, and easily understandable information to the participant [10,12,19]. Participants with diverse educational backgrounds might have difficulties to understand the complexity of the research design and the type of individual research result they may opt for [1,20,21]. For instance, interviews before amyloid disclosure showed how some participants misused the terminology of a positive and negative amyloid PET scan result, whereby the word "positive" was used by participants to describe "good news" and vice versa [14]. The REVEAL study and a recent study with MCI patients after IRR disclosure highlighted that most participants understood the "take-home-message", yet many participants could not recall the specific wording of the result as explained by the study physician [5,15]. Hence, the provided information should not be restricted to a written information brochure. It should also include the opportunity to have a face-to-face conversation with a researcher or study clinician to address any questions and concerns about the study design and the option of being informed of their amyloid PET scan result. The added value of an oral conversation and question moment was mentioned by participants and their carers in the study conducted by Lawrence et al and received positive feedback from amnestic MCI patients in a clinical trial before the amyloid PET disclosure [14,22].

2.1.1. Information provided to the participant

Before trial participation, the following topics need to be explained to the participant [12]: voluntary decision to participate, the right to withdraw throughout the study without having to provide a reason, and to change their mind about being informed of the result [12]. There are two important nuances. First, the participant does not need to provide a reason for altering his/her mind. Although the reason for withdrawal as provided by the participant sometimes provides additional insight and feedback for the research team about the ongoing trial, it can also benefit the research team when designing, setting up, and recruiting for a new trial. Second, participants may change their mind about disclosure up to the moment of disclosure. Once the result has been disclosed, this is an irreversible process the participant needs to be aware off.

In Table 1, we represent benefits and risks as reported by previously conducted studies regarding disclosure of results [14–16,22–27]. Table 1 can provide researchers with an overview of possible benefits and risks, which can be explained to the participant. The benefits and risks should not be limited to the elements mentioned in Table 1, as research is still ongoing to explore more participants' views and concrete experiences on this topic.

Benefits and risks can be interpreted differently by participants compared to the views of researchers [15]. For