Disclosure of APOE Genotype to Asymptomatic Older Adults:

Impact on Subjective and Objective Memory Performance

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Background

- Recent research and debate has focused on the risks, benefits, and general ethics of disclosing APOE genotype to older adults.

- Results of an influential study by Green and colleagues (NEJM 2009) suggest that disclosure has few adverse emotional risks:

  Older adults with a living or deceased parent with AD did not differ in levels of depression or anxiety during the subsequent year, regardless of whether disclosure revealed e4+ or e4- gene status.

- Some argue that few benefits are to be gained by informing asymptomatic adults that they may be at risk for a disease that cannot be prevented or effectively treated.

Background

- The devastating impact of AD on the ability to remember is widely known.

- Knowledge of possession of a characteristic associated with poor cognitive performance can lead to lowered self-efficacy beliefs (i.e., belief in one's capability to produce a given level of performance)

  Activation of negative stereotypes about aging lead to decreased self-efficacy beliefs related to memory ability and decreased test performance in older adults (Levy, J Pers Soc Psych, 1996).

  Higher self-efficacy regarding memory ability is associated with better verbal memory test performance in elderly men (Seeman et al. Psych & Aging, 1996).

Background

Thus, memory test performance might be altered in normal elderly individuals to the extent that knowledge of APOE genotype leads them to question or to have confidence in their memory ability.

Knowing that one has a genotype associated with AD may lead to:

1. Underperformance on objective memory tests due to low confidence.

2. Lower subjective rating of memory ability than in those who do not have the risk or do not know their genotype.

Article

Effect of Knowledge of APOE Genotype on Subjective and Objective Memory Performance in Healthy Older Adults

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Objective: The knowledge that one carries the apolipoprotein E (APOE) ε4 allele risk factor for Alzheimer's disease was recently found to have little short-term psychological risk. The authors investigated the impact of knowledge of carrying the risk allele on subjective ratings of memory and objective memory test performance of older adults.

Method: Using a nested case-control design, the authors administered objective verbal and visual memory tests and self-rating scales of memory function to 144 cognitively normal older adults (ages 52–89) with known APOE genotype who knew (ε4+, N=25; ε4−, N=49) or did not know (ε4+, N=25; ε4−, N=45) their genotype and genetic risk for Alzheimer's disease prior to neuropsychological evaluation.

Results: Significant genotype-by-disclosure interaction effects were observed on several memory rating scales and tests of immediate and delayed verbal recall. Older adults who knew their ε4+ genotype judged their memory more harshly and performed worse on an objective verbal memory test than did ε4+ adults who did not know. In contrast, older adults who knew their ε4− genotype judged their memory more positively than did ε4− adults who did not know, but these groups did not differ in objective memory test performance.

Conclusions: Informing older adults that they have an APOE genotype associated with an increased risk of Alzheimer's disease can have adverse consequences on their perception of their memory abilities and their performance on objective memory tests. The patient's knowledge of his or her genotype and risk of Alzheimer's disease should be considered when evaluating cognition in the elderly.

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Methods and Hypothesis

We obtained subjective memory ratings and tested memory performance in cognitively normal elderly with known APOE genotype who were informed or not informed of their genotype prior to memory evaluation.

Hypotheses:

- Older adults with knowledge of their e4+ status would judge their memory more harshly and have worse objective memory test performance than those without that knowledge.

- Those with knowledge of their e4- status might judge their memory more positively and have better objective memory test performance than those without that knowledge.

Groups

	Ɛ4- Not Informed N=45	Ɛ4- Informed N=49	Ɛ4+ Not Informed N=25	Ɛ4+ Informed N=25
Age	75.0 (6.7)	72.9 (5.1)	72.1 (8.3)	72.6 (5.9)
Education (yrs)	15.9 (2.9)	15.2 (2.2)	15.8 (2.5)	16.0 (2.4)
% Male	51%	41%	40%	44%
MMSE	29.6 (.70)	29.2 (.82)	29.5 (.69)	29.4 (.71)
Mattis DRS	140.4 (2.8)	140.7 (2.9)	141. 4 (2.0)	140.6 (3.1)

Memory Measures

Objective Memory Tests

Logical Memory Test (verbal paragraph recall)

Rey-O Complex Figure Test (visual memory)

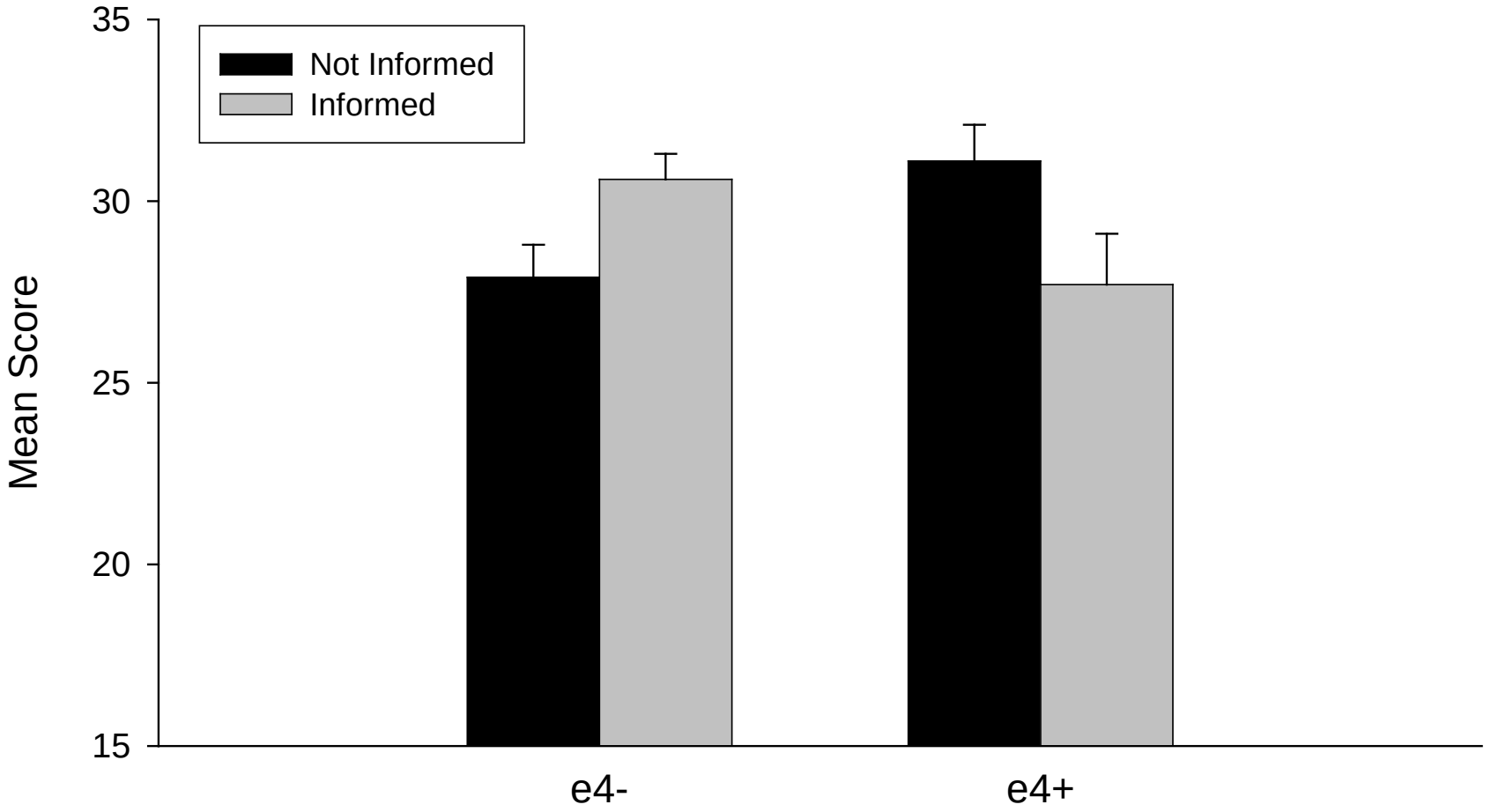
Subjective Memory Ratings

Meta-Memory in Adulthood Questionnaire (MIA)

Memory Functioning Questionnaire

Subjective Memory Ratings

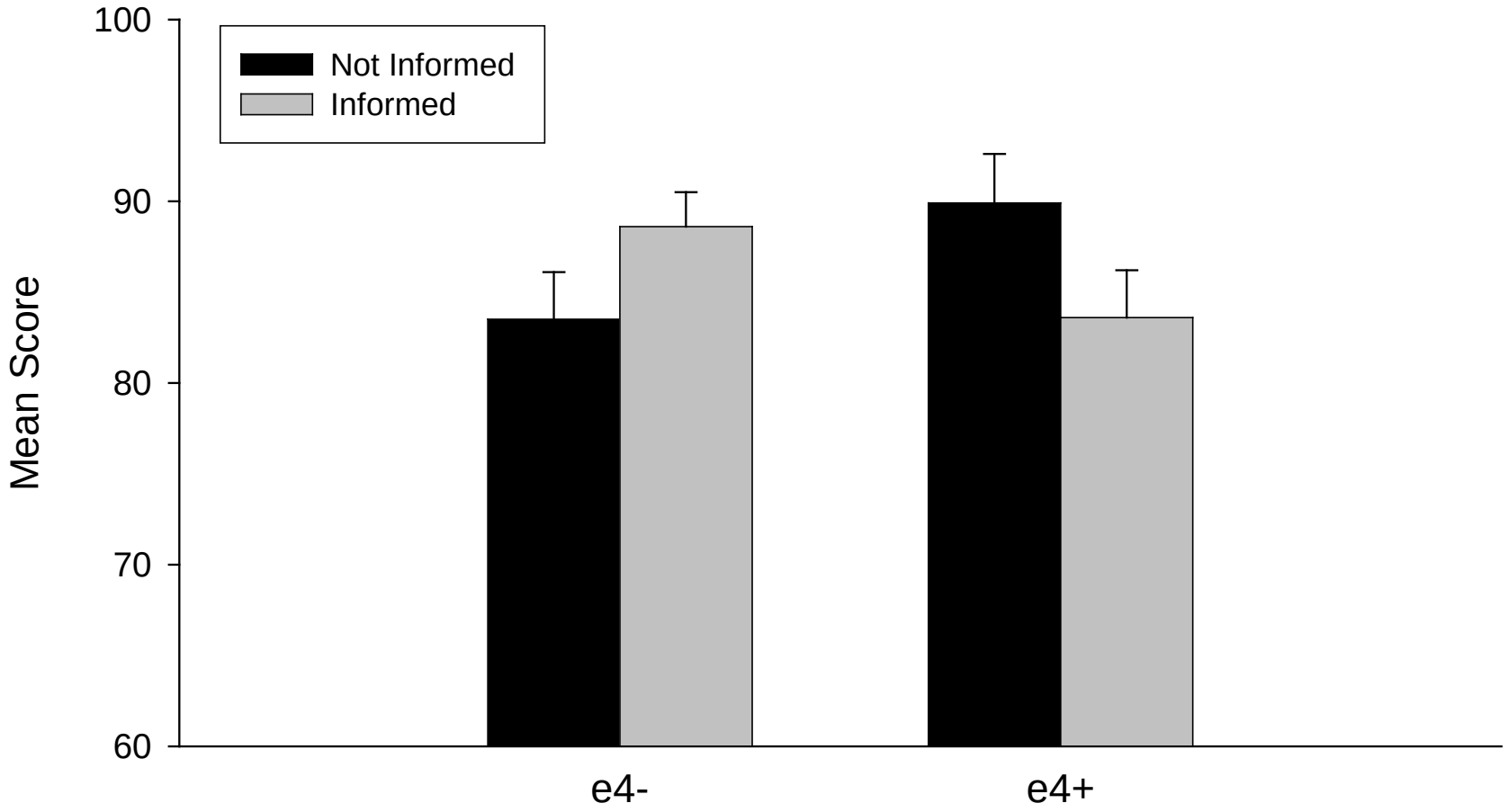
MIA: Capacity Scale



Genotype X Disclosure interaction effects: [F (1, 118) = 7.2, p < .01]

Subjective Memory Ratings

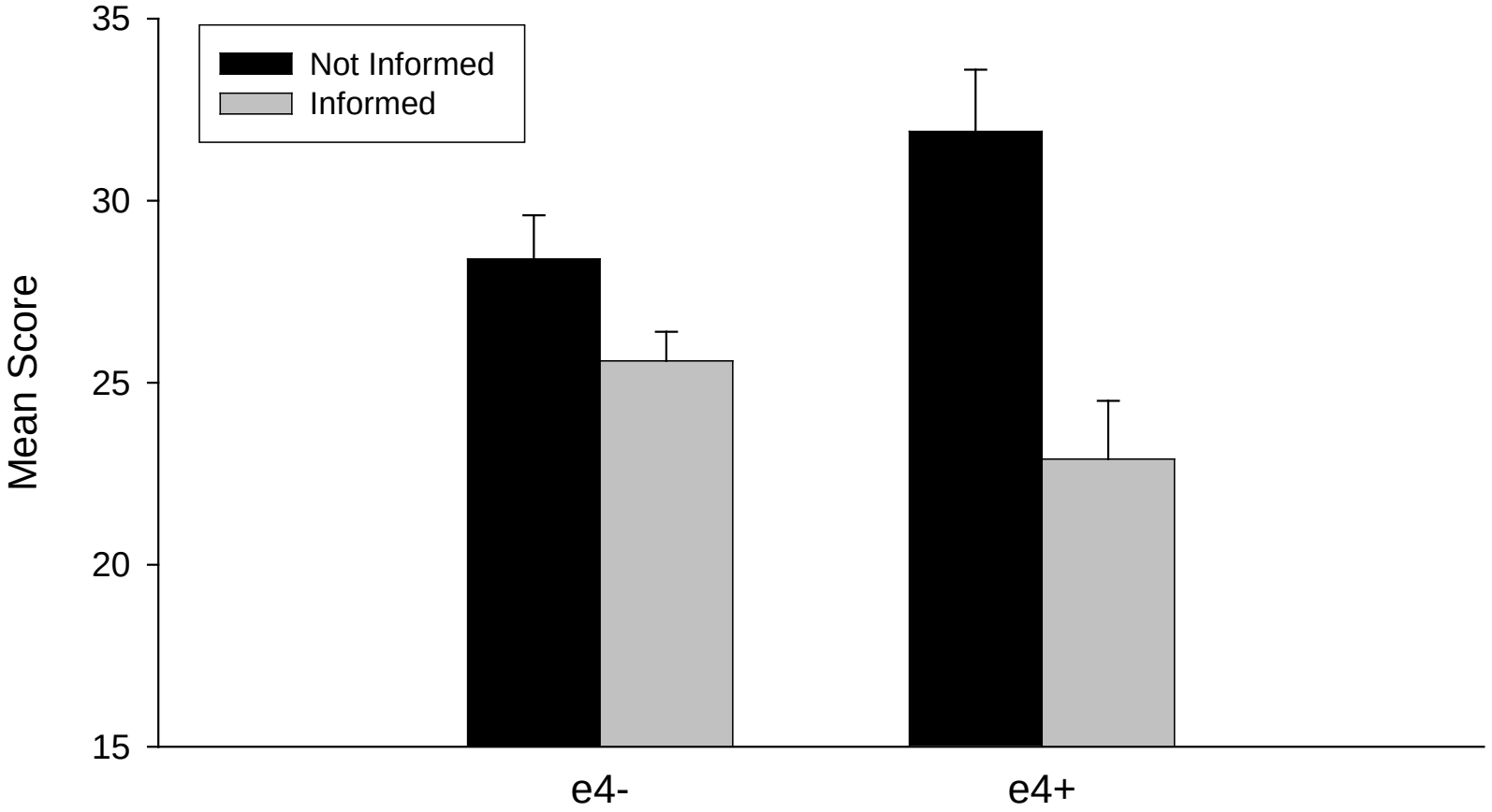
MFQ: Frequency of Forgetting



Genotype X Disclosure interaction effects: [F (1, 118) = 5.6, p < .05]

Objective Memory Ratings

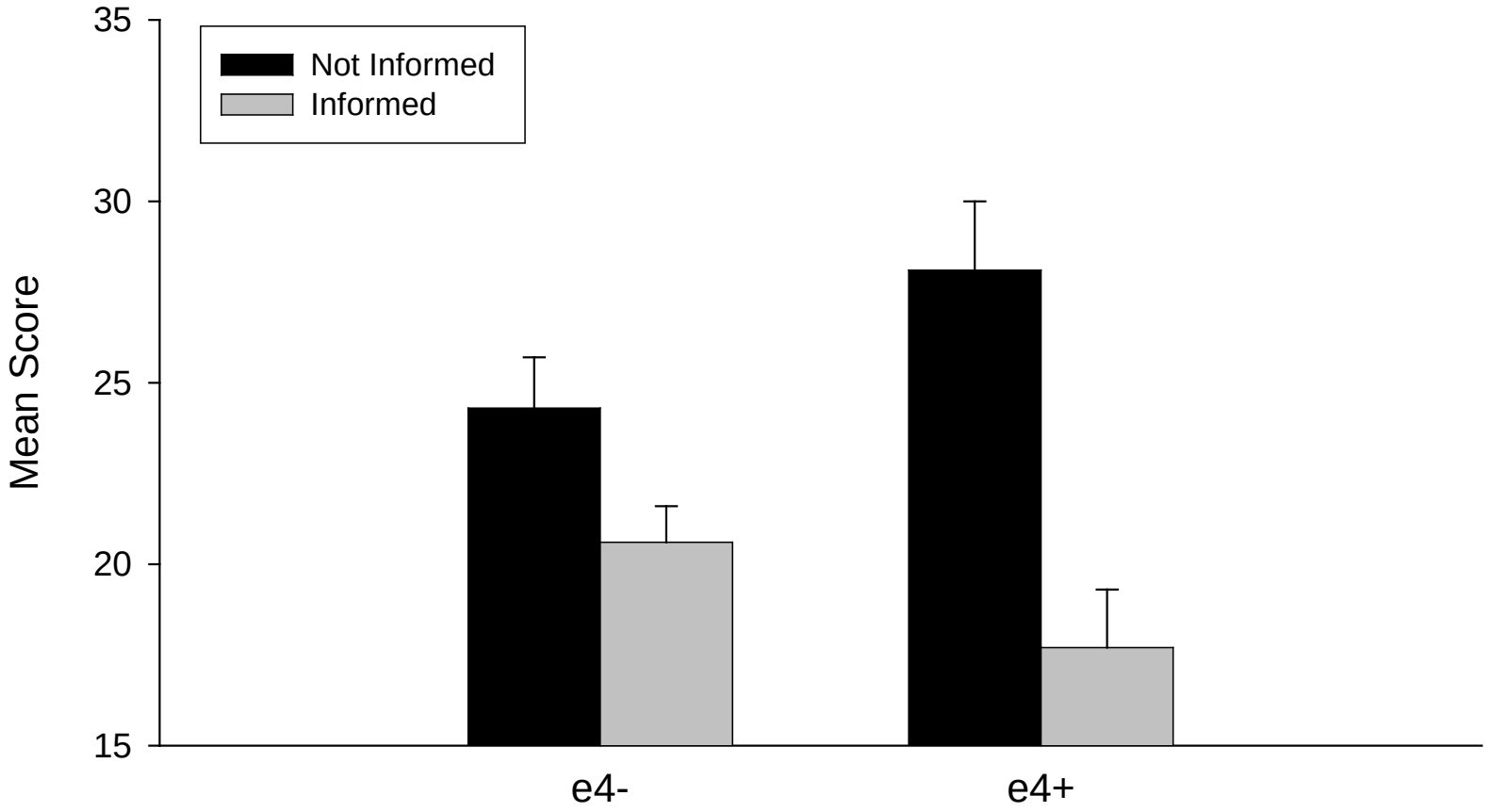
Logical Memory Test: Immediate Recall



Participants who knew they were e4+ performed worse than those who did not know they were e4+. No significant difference in e4- participants who knew or did not know their genotype: [F (1, 110) = 4.7, p < .05]

Objective Memory Ratings

Logical Memory Test: Delayed Recall



Participants who knew they were e4+ performed worse than those who did not know they were e4+. No significant difference in e4- participants who knew or did not know their genotype: [F (1, 110) = 4.3, p < .05]

Geriatric Depression Scale

	Ɛ4- Not Informed N=45	Ɛ4- Informed N=49	Ɛ4+ Not Informed N=25	Ɛ4+ Informed N=25
GDS Score	5.0 (4.8)	4.6 (4.2)	3.5 (4.3)	3.3 (2.9)

Conclusions

- Disclosure of an e4+ genotype can have adverse consequences on subjective self-ratings and objective tests of memory in cognitively normal older adults.

- These results could be related to lower self-efficacy beliefs regarding memory in those with knowledge that they are at increased risk for AD (stereotype threat, self-fulfilling prophecy).

- Those who know they are at risk may have lowered expectations which results in reduced persistence and effort in performing memory tasks, or reduced time spent on memory tasks that are perceived as difficult.

Clinical Implications

- Similar consequences might be expected if other indices of increased AD risk are disclosed (e.g., neuroimaging or CSF biomarkers of preclinical AD).

- Such knowledge could have a serious clinical impact by increasing the likelihood of false-positive diagnosis of dementia or MCI in those who know they are e4+.

- It could also distort the results of AD primary prevention clinical trials if those with knowledge of e4+ status are over-represented in an unbalanced way in either the placebo or treatment arm of a trial.

Future Considerations

- These adverse consequences of knowledge of e4+ genotype might be reduced by psychological interventions.

- A number of studies show that negative stereotypes regarding cognitive abilities can be overcome to improve performance (Cohen et al., Science, 2006; Science 2009).

- Interventions that mitigate negative self-perception of cognitive abilities might be useful in reducing the adverse effects of knowledge of e4+ genotype in older individuals.

How and why should results of predictive testing for AD be disclosed to asymptomatic older adults?

Predictive Testing: Lessons from HD

1. **The individual is empowered to make the decision to receive the information.**

- The decision to take the test and learn the results is the sole choice of the person concerned.
- The person must be given up to date, relevant information in order to make an informed voluntary decision.

2. **The counseling /testing process is structured.**

- The counseling team is multidisciplinary, with personnel (e.g., clinical genetic counselor) trained to impart knowledge and provide support.
- Pre- testing and Post- testing counseling are essential.

Predictive Testing: Lessons from HD

3. **The counseling /testing process is personalized.**

- Can the person handle the results?
- Should a companion be required?
- Information on consequences of having a positive or negative test
- Age of onset questions
- Implications for family

Disclosing AD Risk

Positives

- Ability to prepare for the future
- Existence of life style changes that may postpone onset

Negatives

- possibility of adverse reaction
- Current treatments have a modest effect on disease progression
- widespread testing may result in increased healthcare costs
- discrimination in terms of employability and insurability

Disclosure of AD Risk: the literature

- Most would like to have the choice, particularly if there are potential strategies (e.g., exercise) for reducing risk.
- Distress vs. relief in response varies widely; many react positively, but there are always exceptions.
- Test-related distress and behavioral changes increase in e4+.
- Level of information about what the results mean vary widely.
- Risk estimates vary depending on sample type and methodology.
- Telephone disclosure is generally safe.
- Including a companion in the disclosure process is recommended.
- Little to no indication of how e4+,e4+ respond to disclosure.

Questions around AD disclosures

- What information should we impart (risk estimates vary)?
- How can new research findings be disseminated to disclosing professionals?
- Is discrimination a risk after testing?
- What is optimal structure of testing, disclosure, and follow-up?
- How do we avoid giving unwanted information?

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