Ethically Evaluating Research involving the Engraftment of Human Neural Stem Cells in Nonhuman Primates

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Ethical Issues

- Informed Consent Issues
- Traditional Animal Ethics Concerns
- The Moral Status Framework

- Reserve for discussion period
  - The Unnaturalness Argument
  - The Moral Confusion Argument
  - The Human Dignity Argument
  - Considerations of Political Legitimacy

Donors and the Public Care about Consent

- "The 30 studies provide data on the views of more than 33,000 people. The studies assessed the views of patients, research participants, family members, religious leaders, and the public. The studies yield consistent findings, despite being conducted around the world, over a 10 year period, in different groups, using different methods. *Most respondents want to decide whether their samples are used for research purposes.*" (Wendler 2006; italics added)

Concerns about Donating Surplus Embryos

- Syrop et al. (1995): Only 9% chose to donate surplus embryos for research; 44% chose discard over donation to research
- McMahon et al. (2003): Only 10% probable, 34% possible, said they would donate their surplus embryos for research
- Bangsbøll et al. (2004): Only 57% expressed willingness to donate surplus embryos for hESC research
- Lyerly and Faden (2007): Only 50% of couples with cryopreserved embryos would be willing to donate surplus embryos for hESC research

Social Science Research on Transgenics

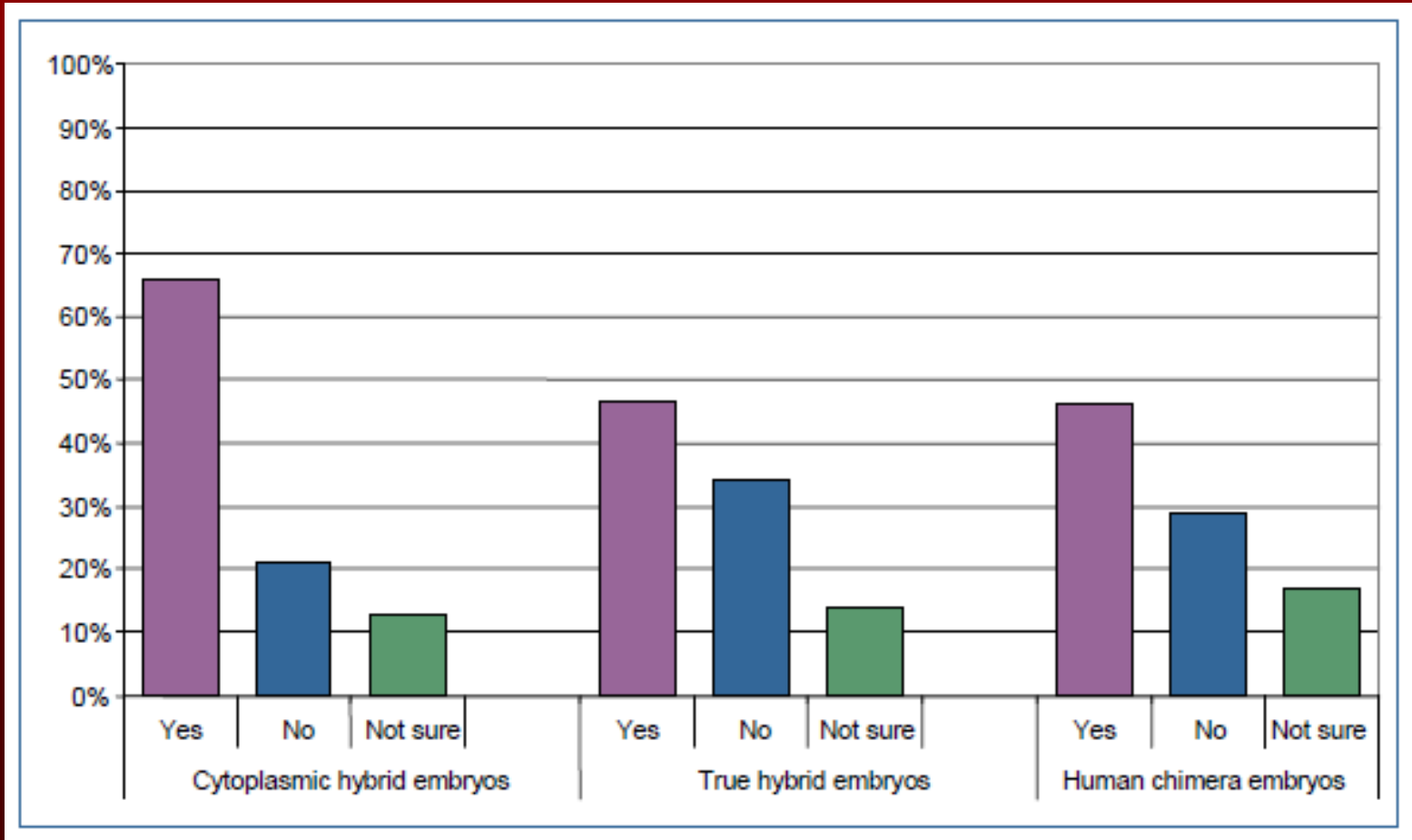
Source	Plants	Animals
OTA (1987)	6.6 (out of 10) average acceptability with genetically modifying plant cells	5.3 with animal cells
Hoban et al. (1992)	23% opposed plant GE	53% opposed animal GE
Rutgers Food Policy Institute (2002)	37% disapproved strongly or somewhat of GE plants; 22% said it was wrong	68% disapproved strongly or somewhat of GE animals; 55% said it was wrong
Pew (2003)	6.08 mean comfort level	2.81 mean comfort level
Pew (2003)	81% said that producing more affordable pharmaceuticals was a good reason to genetically modify plants; 14% said it was a bad reason	49% said that it was a good reason; 42% said it was a bad reason

UK Social Science Research on Mixed Embryos

Source	Finding
UK Dept of Health Review of the HFEA (2006)	"[T]here is considerable public unease with the possible creation of embryos combining human and animal material...."
Baylis (2009) on HFEA Consultation Process	"[T]he data from three of the four [HFEA] consultation mechanisms showed 67 percent, 48 percent, and 47 percent "against" humanesque cytoplasmic hybrid embryo research, compared with 17.5 percent, 35 percent, and 39 percent "for" such research. (There are no percentages reported for the deliberative work [with 44 participants])."

Concern about Animal/Human Mixing even among Supporters of Embryo Research

HFEA 2007: Response of those not generally opposed to embryo research to the question of whether the HFEA should license ...



Ethical Implications

- One of the most important functions of the requirement for informed consent is to avoid implicating donors in research activities that they would find morally problematic.
- Specific informed consent is morally required for research that a significant proportion of potential donors can be expected to find morally problematic.
- Neural stem cells should only be introduced into an NHP with the specific informed consent of the donors of any embryos, gametes, fetal tissue, or somatic cells from which the neural stem cells are derived.

Traditional Animal Ethics Issues

- How harmful is the research to the nonhuman primates?
- To what extent are the harms of the research necessary for generating valuable benefits and knowledge?
- To the extent that there is a genuine conflict of interests, is the moral status of the NHPs sufficiently low compared to that of humans that it is permissible to sacrifice their interests for ours?

(Net?) Harm to NHPs

- Comprehensive accounting, including but not limited to:
  - Confinement
  - Limited social contact and enrichment
  - Medical procedures
  - Premature death
  - Access to some opportunities for enrichment
  - Access to food, veterinary care
  - Shelter from risks of natural environment
  - Existence (?)
  - Probabilities

Benefits and Knowledge

- Are the harms "necessary"?
  - Do alternative means to the same end exist?
  - How do the alternative means compare to the proposed research?
  - Could the resources be used to achieve a different end that compares favorably to the proposed research?
- How valuable are the benefits or knowledge?
  - Scientific validity of the research design
  - Value of valid results
- Probabilities

Views of NHPs' Moral Status

- Views of NHPs' moral status can be categorized by the importance of the human interests they claim it would take to justify sacrificing the fundamental interests of NHPs
  - Fundamental Interest: Failure to satisfy makes it difficult to live even a minimally decent life
  - Significant Interest: Failure to satisfy has a significant negative impact on one's ability to flourish
  - Minimal Interest: Failure to satisfy does not significantly impact one's ability to flourish

Views of NHPs' Moral Status

- Minimal Moral Status: It is permissible to sacrifice the fundamental interests of an NHP if doing so is necessary for satisfying minimal human interests.
- Significant Moral Status: It is permissible to sacrifice the fundamental interests of an NHP only if doing so is necessary for satisfying significant human interests.
- Fundamental Moral Status: It is permissible to sacrifice the fundamental interests of an NHP only if doing so is necessary for satisfying fundamental human interests.
- N.B.: Need consideration of the numbers involved.

Views of NHPs' Moral Status

- Equal Moral Status: Sacrificing an interest of an NHP is only justified by considerations that would also justify the sacrifice of an equally weighty interest of a human being to whom the agent had no special obligations or special relationships.

  - Utilitarian Views
  - Consequentialist Views
  - Pro Tanto Deontological Views
  - Absolutist Deontological Views

Capacities Relevant to Moral Status?

- Sentience
- Self-awareness
- Sociability
- Rationality
- Language
- Moral Autonomy
- ...

- Potential for _____
- Past, present, or future possession of _____

- Membership in the species *Homo sapiens*

The Moral Status of NHPs

- On any reasonable view, all NHPs have at least Significant Moral Status
- Enculturated, linguistically-trained NHPs probably have (something close to) Equal Moral Status
- Whether other NHPs merely have Significant Moral Status, or have Fundamental or Equal Moral Status turns on:
  - Ethical facts about the basis, measurement, and form of moral status
  - Empirical facts about morally relevant properties of NHPs
- Research does not strongly support a sharp division between (a) great apes and (b) gibbons and monkeys

Ethical Implications

- Impermissible to introduce human neural stem cells into enculturated, linguistically-trained NHPs
- Not clear that there is any reason, based on traditional animal ethics concerns, for singling out this kind of research compared to other invasive biomedical research on NHPs

The Moral Status Framework

- Suppose you think that traditional animal ethics concerns yield the result that engrafting is permissible because NHPs have a sufficiently low degree of moral status compared to humans.

- Then you face a further ethical question:

  – Could the introduction of human neural stem cells into an NHP result in its acquiring the biological or psychological properties that suffice for Equal Moral Status?

Current Research Is Unlikely to Enhance Status

- Smaller skull size
- Already fixed brain architecture
- Surrounding non-human cellular environment
- Small numbers of human cells being introduced, compared to the number of animal cells
- Poor viability and integration of cells
- Shorter gestational periods
- Early termination/non-viability

But What about ...

- ... introducing large numbers of hPS cells into an NHP embryo that will be brought to term?
  - NAS (2005): “It is not now possible to predict the extent of human contribution to such chimeras”
- Research with the goal of creating animals with properties that are relevant to moral status
  - Basic research on physical or psychological basis of properties relevant for moral status
  - Generation of animal models to study diseases or injuries that affect properties relevant for moral status

Evaluating Status Enhancements

- An enhancement in moral status is ethical only if the researchers provide reasonable assurances that the individual's new moral status will be adequately respected.
  - Not enough to treat it the same.
  - Not even enough to treat it somewhat better.
- Analogy with procreative ethics

The Outcome to be Avoided

- A situation in which a transplant of human neural stem cells into an NHP really does render the individual the moral equivalent of a normal adult human ...
- ... and the individual continues being treated as animals are usually treated in biomedical research.

Ethical Implications

- In all plausible research contexts, satisfying this requirement will be incompatible with the research goals that motivated the use of NHPs instead of humans.
  - Unwilling subjects
  - Non-therapeutic, significantly risky interventions
  - Life-long confinement
- More general point: researchers affecting an NHP's moral status or altering the interests of which they are capable need to be cognizant of and responsible for any morally required changes in the treatment of the NHP

Review

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