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Submit only ONE copy of this form **for each PI/PD and co-PI/PD** identified on the proposal. The form(s) should be attached to the original proposal as specified in GPG Section II.B. Submission of this information is voluntary and is not a precondition of award. This information will not be disclosed to external peer reviewers. ***DO NOT INCLUDE THIS FORM WITH ANY OF THE OTHER COPIES OF YOUR PROPOSAL AS THIS MAY COMPROMISE THE CONFIDENTIALITY OF THE INFORMATION.***

PI/PD Name: Matthew K Belmonte

Gender: ☐ Male ☐ Female

Ethnicity: (Choose one response) ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Race:
(Select one or more)
☐ American Indian or Alaska Native
☐ Asian
☐ Black or African American
☐ Native Hawaiian or Other Pacific Islander
☐ White

Disability Status:
(Select one or more)
☐ Hearing Impairment
☐ Visual Impairment
☐ Mobility/Orthopedic Impairment
☐ Other
☐ None

Citizenship: (Choose one) ☐ U.S. Citizen ☐ Permanent Resident ☐ Other non-U.S. Citizen

Check here if you do not wish to provide any or all of the above information (excluding PI/PD name): ☒

Pecase Eligibility: Y

REQUIRED: Check here if you are currently serving (or have previously served) as a PI, co-PI or PD on any federally funded project ☐

Ethnicity Definition:
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Race Definitions:
American Indian or Alaska Native. A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.
Asian. A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
Black or African American. A person having origins in any of the black racial groups of Africa.
Native Hawaiian or Other Pacific Islander. A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
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The Federal Government has a continuing commitment to monitor the operation of its review and award processes to identify and address any inequities based on gender, race, ethnicity, or disability of its proposed PIs/PDs. To gather information needed for this important task, the proposer should submit a single copy of this form for each identified PI/PD with each proposal. Submission of the requested information is voluntary and will not affect the organization's eligibility for an award. However, information not submitted will seriously undermine the statistical validity, and therefore the usefulness, of information recieved from others. Any individual not wishing to submit some or all the information should check the box provided for this purpose. (The exceptions are the PI/PD name and the information about prior Federal support, the last question above.)

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List of Suggested Reviewers or Reviewers Not To Include (optional)

SUGGESTED REVIEWERS:

Annette Karmiloff-Smith, University College London
Mark Johnson, University College London
Uta Frith, University College London
Tony Charman, University College London
Laurent Mottron, UniversitØ de MontrØal
John Foxe, City University of New York
Dave Woods, University of California Davis

Any reviewer previously assigned to NSF-SBE-BCS CAREER proposal 0746922 submitted July 2007.

REVIEWERS NOT TO INCLUDE:

Not Listed

COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

PROGRAM ANNOUNCEMENT/SOLICITATION NO./CLOSING DATE/if not in response to a program announcement/solicitation enter NSF 08-1		FOR NSF USE ONLY
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AWARDEE ORGANIZATION CODE (IF KNOWN) 0027110001	
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IS AWARDEE ORGANIZATION (Check All That Apply) (See GPG II.C For Definitions)
☐ SMALL BUSINESS ☐ MINORITY BUSINESS
☐ FOR-PROFIT ORGANIZATION ☐ WOMAN-OWNED BUSINESS
☐ IF THIS IS A PRELIMINARY PROPOSAL THEN CHECK HERE

TITLE OF PROPOSED PROJECT **CAREER: Integrative Behavioural and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments**

REQUESTED AMOUNT	PROPOSED DURATION (1-60 MONTHS)	REQUESTED STARTING DATE	SHOW RELATED PRELIMINARY PROPOSAL NO. IF APPLICABLE
$ 855,955	60 months	06/01/09	

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☒ BEGINNING INVESTIGATOR (GPG I.G.2)
☐ DISCLOSURE OF LOBBYING ACTIVITIES (GPG II.C)
☐ PROPRIETARY & PRIVILEGED INFORMATION (GPG I.D, II.C.1.d)
☐ HISTORIC PLACES (GPG II.C.2.j)
☐ SMALL GRANT FOR EXPLOR. RESEARCH (SGER) (GPG II.D.1)
☐ VERTEBRATE ANIMALS (GPG II.D.5) IACUC App. Date ________
PHS Animal Welfare Assurance Number ________
☒ HUMAN SUBJECTS (GPG II.D.6) Human Subjects Assurance Number ________
Exemption Subsection ________ or IRB App. Date Pending
☐ INTERNATIONAL COOPERATIVE ACTIVITIES: COUNTRY/COUNTRIES INVOLVED (GPG II.C.2.j)
____
☐ HIGH RESOLUTION GRAPHICS/OTHER GRAPHICS WHERE EXACT COLOR REPRESENTATION IS REQUIRED FOR PROPER INTERPRETATION (GPG I.G.1)

PI/PD DEPARTMENT	PI/PD POSTAL ADDRESS
Human Development	G77 Martha Van Rensselaer Hall Ithaca, NY 148534401 United States
PI/PD FAX NUMBER 607-255-9856	

NAMES (TYPED)	High Degree	Yr of Degree	Telephone Number	Electronic Mail Address
PI/PD NAME Matthew K Belmonte	DPhil	2001	607-255-6385	mkb4@cornell.edu
CO-PI/PD				
CO-PI/PD				
CO-PI/PD				
CO-PI/PD				

CERTIFICATION PAGE

Certification for Authorized Organizational Representative or Individual Applicant:

By signing and submitting this proposal, the Authorized Organizational Representative or Individual Applicant is: (1) certifying that statements made herein are true and complete to the best of his/her knowledge; and (2) agreeing to accept the obligation to comply with NSF award terms and conditions if an award is made as a result of this application. Further, the applicant is hereby providing certifications regarding debarment and suspension, drug-free workplace, and lobbying activities (see below), nondiscrimination, and flood hazard insurance (when applicable) as set forth in the NSF Proposal & Award Policies & Procedures Guide, Part I: the Grant Proposal Guide (GPG) (NSF 08-1). Willful provision of false information in this application and its supporting documents or in reports required under an ensuing award is a criminal offense (U. S. Code, Title 18, Section 1001).

Conflict of Interest Certification

In addition, if the applicant institution employs more than fifty persons, by electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative of the applicant institution is certifying that the institution has implemented a written and enforced conflict of interest policy that is consistent with the provisions of the NSF Proposal & Award Policies & Procedures Guide, Part II, Award & Administration Guide (AAG) Chapter IV.A; that to the best of his/her knowledge, all financial disclosures required by that conflict of interest policy have been made; and that all identified conflicts of interest will have been satisfactorily managed, reduced or eliminated prior to the institution's expenditure of any funds under the award, in accordance with the institution's conflict of interest policy. Conflicts which cannot be satisfactorily managed, reduced or eliminated must be disclosed to NSF.

Drug Free Work Place Certification

By electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative or Individual Applicant is providing the Drug Free Work Place Certification contained in Exhibit II-3 of the Grant Proposal Guide.

Debarment and Suspension Certification

(If answer "yes", please provide explanation.)

Is the organization or its principals presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal department or agency? Yes ☐ No ☒

By electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative or Individual Applicant is providing the Debarment and Suspension Certification contained in Exhibit II-4 of the Grant Proposal Guide.

Certification Regarding Lobbying

The following certification is required for an award of a Federal contract, grant, or cooperative agreement exceeding $100,000 and for an award of a Federal loan or a commitment providing for the United States to insure or guarantee a loan exceeding $150,000.

Certification for Contracts, Grants, Loans and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan, or cooperative agreement, the undersigned shall complete and submit Standard Form-LLL, ''Disclosure of Lobbying Activities,'' in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into this transaction imposed by section 1352, Title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than $10,000 and not more than $100,000 for each such failure.

Certification Regarding Nondiscrimination

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Two sections of the National Flood Insurance Act of 1968 (42 USC §4012a and §4106) bar Federal agencies from giving financial assistance for acquisition or construction purposes in any area identified by the Federal Emergency Management Agency (FEMA) as having special flood hazards unless the:

(1) community in which that area is located participates in the national flood insurance program; and
(2) building (and any related equipment) is covered by adequate flood insurance.

By electronically signing the NSF Proposal Cover Sheet, the Authorized Organizational Representative or Individual Applicant located in FEMA-designated special flood hazard areas is certifying that adequate flood insurance has been or will be obtained in the following situations:

(1) for NSF grants for the construction of a building or facility, regardless of the dollar amount of the grant; and
(2) for other NSF Grants when more than $25,000 has been budgeted in the proposal for repair, alteration or improvement (construction) of a building or facility.

AUTHORIZED ORGANIZATIONAL REPRESENTATIVE	SIGNATURE	DATE
NAME		

TELEPHONE NUMBER	ELECTRONIC MAIL ADDRESS	FAX NUMBER

*SUBMISSION OF SOCIAL SECURITY NUMBERS IS VOLUNTARY AND WILL NOT AFFECT THE ORGANIZATION'S ELIGIBILITY FOR AN AWARD. HOWEVER, THEY ARE AN INTEGRAL PART OF THE INFORMATION SYSTEM AND ASSIST IN PROCESSING THE PROPOSAL. SSN SOLICITED UNDER NSF ACT OF 1950, AS AMENDED.

COVER SHEET FOR PROPOSAL TO THE NATIONAL SCIENCE FOUNDATION

FOR CONSIDERATION BY NSF ORGANIZATION UNIT(S) - continued from page 1
(Indicate the most specific unit known, i.e. program, division, etc.)

BCS - DEVELOP& LEARNING SCIENCES/CRI

CAREER ELIGIBILITY CERTIFICATIONS

A. CAREER ELIGIBILITY CERTIFICATION

To be eligible for a CAREER award, you must meet the CAREER eligibility requirements as defined in the CAREER Program Solicitation (also refer to the CAREER FAQ for further explanations). To certify your eligibility, complete each section of the CAREER checklist below. The CAREER Eligibility Certification checklist will be included as part of the proposal and will be sent to reviewers.

I certify that by the relevant July deadline for submission of CAREER proposals, I will have met all of the following criteria.

- ☒ I will hold a doctoral degree in a field of science or engineering supported by NSF
- ☒ I will be untenured
- ☒ I will not have received an NSF PECASE or CAREER award
- ☒ I will not have competed more than two times in previous NSF CAREER Program Competitions

I certify that by October 1st following the relevant July deadline for submission of CAREER proposals I will

☒ be employed in a tenure-track position

OR

☐ be employed in a tenure-track equivalent position

☒ hold the title of assistant professor

OR

☐ hold a title that is equivalent to assistant professor

☒ be employed at an institution in the U.S., its territories, or possessions, or the Commonwealth of Puerto Rico that awards degrees in a field of science or engineering supported by NSF

OR

☐ be employed at an institution in the U.S., its territories, or possessions, or the Commonwealth of Puerto Rico that is a non-profit, non-degree granting institution such as a museum, observatory, or research lab

CAREER: Integrative Behavioural and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments – PROJECT SUMMARY

How do attention, perceptual organisation, executive function and social cognition relate to each other developmentally, and what are the neurophysiological underpinnings of this relationship in contexts of normal and abnormal development? This question is of great relevance to the wider discipline of cognitive neuroscience, and huge broader relevance to families, educators, and other caregivers struggling to cope with the consequences of developmental disorders. Discovering the answers depends on asking the right integrative questions that cut across theoretical paradigms. This proposal combines behavioural and physiological studies of normal and autistic children, within perceptual, attentional, executive, and social cognitive domains of functioning – domains which historically have remained largely separate in research on developmental disorders. The project creates research applications within undergraduate curricula in developmental cognitive neuroscience and in computing and information science, adding a practical component to an existing course on autism and the development of social cognition, and supporting a practicum in software design for the video games industry.

<u>Intellectual Merit:</u> This integrative study is proposed not simply as an end in itself but also as a vehicle for research and instruction in broader areas of cognitive neuroscience. Developmental disorders in general, and autism in particular, are a timely focus for such investigations because of their relation to current interests in neural connectivity. This group's and others' investigations point to a model of autism not as an anatomically and developmentally isolated lesion, but as a pervasive alteration of neural information processing in which abnormal local network connectivity within brain regions perturbs the development of longer-range connectivity between brain regions. Understanding how these dynamics play out in normal and abnormal brain and cognitive development demands a synthetic view that integrates behavioural and physiological observations across cognitive domains, and one that takes into account endophenotypes in order to examine how predisposing factors are developmentally translated into the full disease syndrome. These goals will be accomplished by implementing a suite of perceptual and cognitive experiments in the context of a video game – a more motivating and ecologically valid environment than many other experimental settings. In addition to children with autism and unrelated normal controls, the project will evaluate clinically normal siblings of people with autism in order to refine previous findings relating behavioural and neurophysiological endophenotypic traits. The physiological component of these studies takes advantage of new developments in high-impedance, low preparation time EEG hardware, and applies new analytical techniques that make use of all the information available in high-density EEG recordings and explicitly address brain connectivity via measures of phase coherence between EEG sources.

<u>Broader Impact</u>: The subject of developmental disorders motivates and engages students and communities as few others can do, and this topic fits well with the land-grant mission of Cornell's College of Human Ecology to apply research to real-world challenges. The proposed project would add an undergraduate research component to the existing course "Autism and the Development of Social Cognition," using the lens of autism to explore the more general question of the how complex social cognitive skills may emerge developmentally from more elementary neural properties. This popular course enrols a mix of highly motivated students with ambitions in medicine, clinical psychology, neurobiology, and early childhood education. In addition, the project would provide an undergraduate practicum in the Game Design Initiative at Cornell (GDIAC), a curriculum that integrates computer science and the arts in preparing students for work in the video games industry. There is very substantial curiosity about neuroscience and enthusiasm for this work amongst GDIAC students. Perhaps most significantly, the project would form a nucleus for outreach efforts to disseminate the latest neuroscientific knowledge to students, parents, teachers, and other stakeholders in central New York's education community. Teachers want to know how children process information – how do anxiety and compulsive behaviours interact with a student's ability to stay on task, how is learning style affected by difficulties in shifting attention and integrating perceptual channels, and what specific topics and approaches are likely to appeal to students' individual cognitive styles? Parents want to know which treatments have any scientific support or scientific plausibility – is there any truth to popular rhetorics about autism, for instance its description as a deficit of "sensory integration," and should families spend large amounts of money on unproven therapies? Geographically isolated from the academic centres of major cities, central New York has particular need for this sort of involvement of science in the community.

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For font size and page formatting specifications, see GPG section II.C.

Appendix Items:

*Proposers may select any numbering mechanism for the proposal. The entire proposal however, must be paginated. Complete both columns only if the proposal is numbered consecutively.

PROJECT DESCRIPTION

1. BACKGROUND AND PRELIMINARY SUPPORTING DATA

1.0 Response to Reviewers

Several modifications and updates have been made in response to the recommendation from last year's panel that "if the proposal is not funded in this round then a new proposal with clarification of issues of concern should be submitted."

1. The time line for video game development and data collection in parallel would have precluded the performance of all tasks by all subjects. Time has solved this issue. The video game is being completed and piloted using a small grant from Autism Speaks, and will be fully implemented in fall 2008, well before the start date of the current proposal. The only development remaining will be that associated with the supplementary tasks to be proposed in student projects, part of the education component of this proposal. These student projects will complement and extend the proposed research, but are not essential to it and need not be run on all subjects.

2. The number of subjects was less than what might be needed for the proposed correlational analyses, and might not yield complete data on all tasks till the end of the time frame. Especially given the cost of magnetic resonance imaging, this issue is a delicate balance between investigational size and completeness on the one hand, and budgetary realism on the other. The budget has been expanded to accommodate 24 subjects (8 per group) per year, which will be pooled with EEG and behavioural data currently being collected from an additional 10 subjects per group as part of the aforementioned pilot grant from Autism Speaks.

3. Inclusion, diagnostic and matching criteria were not completely specified. These details are now added.

4. The PI needs an experienced senior consultant to advise on management of the project and of the students involved in it. Such a consultancy has been arranged with Professor Steve Robertson (see letter attached). Also, the aforementioned Autism Speaks pilot funding for undergraduates in game development now frees this proposal to focus on more senior personnel who will assist with data acquisition and analysis.

5. Who will coordinate recruitment, scheduling and data management? Attached are letters from Dr Barbara Ganzel, who has been coordinating these aspects of the project and will continue to do so, and from Karen Fried, director of autism services at the Franziska Racker Centers who will be assisting with subject recruitment.

6. The proposal needs details on the actual procedures. Details on testing, personnel, piloting of student projects from the Game Design Initiative, and technical aspects of EEG recording and analytical procedures have been added.

7. At least one additional research assistant is probably needed. A line for a postdoctoral fellow with experience in EEG recording and data analysis has been added. In addition, the project benefits from the services of Dr Ganzel as detailed in #5 above, and from several undergraduate research assistants trained by the PI.

8. There was no specific justification of the 10-15 year age range. A rationale has been added.

9. The video games seem male-oriented. Part of this impression may arise from the design of the game to appeal to children with autism, since autistic children tend to excel in certain cognitive domains associated socially or biologically with male gender or sex (Baron-Cohen 2002). With that said, this critique has been taken to heart and the remaining two mini-games, as well as the colony-fostering framework of the game, have been redesigned so as to eschew the male-oriented, "shooter" paradigm, with consultation from female and male experts in the Game Design Initiative and reference to formal studies of ungendered game design (Graner Ray 2004). The new designs are described in the methods below.

1.1 Autism as a Vehicle for Integrative Cognitive Neuroscience

This proposal is founded on the notion that understanding what goes wrong in autistic development can help us to understand what goes right in normal development. Autism research has in recent years gained currency in cognitive neuroscience because of its direct relevance to an evolving focus on network-level analyses, and because of a recognition of the importance of developmental interactions in the formation and specification of cognitive systems (Karmiloff-Smith 2007). This theoretical paradigm of interactive specialisation provides an alternative both to a strictly modular view of cognition and to a strictly equipotential view, positing that cognitive capacities that may seem unitary and modular in normally developed adults may arise in the developmentally programmed, but activity-dependent, interactions of more elementary capacities. In this perspective, the emergence of new skills during development depends not on the independent maturation of individual cognitive modules, nor exclusively on the acquisition of expertise by domain-general processing systems, but rather in activity-dependent interactions that tune neural responses, refining the capabilities of cognitive subsystems and altering functional connectivity between brain regions. The relation of elementary to complex cognitive capacities in the context of disordered development thus provides a natural experimental framework within which to explore the developmental consequences of these interactions (Johnson et al. 2005).

The value of the proposed project stems from its integrative approach to relating low-level perturbations of attention and perception to higher-level social cognitive abnormalities, aiming to explore this relation of complex emergent capacities to developmentally simpler antecedents, both in the more evident context of disordered development and also in the context of normal cognitive variation. The project combines behavioural and physiological measures across a wide range of levels of cognitive processing, multivariate analytical methods that address functional connectivity, and a subject pool that includes not only normal children but also developmentally disordered children and their clinically unaffected siblings. These methods and comparisons confer an ability to identify and to differentiate those neurophysiological traits associated with familial liability to disordered brain and cognitive development from those associated with developmental disorder *per se,* to suggest how the former may be developmentally translated into the latter, and thus to shed light on the general question of how individual variants interact with normal programmes and gradients of brain and cognitive maturation to determine developmental endpoints.

The broader impact of basic science proposals often can seem remote – especially in child neuropsychiatric applications such as autism, where so many promises have been made and, at least historically, so little delivered to families who are trying to cope with the daunting and all-consuming occupation of raising a developmentally disordered child. This research group regards this question of relevance as crucial, and the problem of neurodevelopmental disorders as an ongoing and accelerating tragedy that demands cognitive neuroscience's urgent attention and cooperation. The application of cognitive neuroscience to developmental disorders has immediate relevance for people with autism spectrum conditions who want to exploit a better understanding of how their minds operate, for parents who are often presented with unproven treatments for their autistic children, for therapists and educators who want to understand how autism's pattern of cognitive strengths and weaknesses determines each individual's learning style, and for students of cognitive neuroscience who wish to apply and to refine their knowledge in the context of a real-world problem on which they can have great impact. This proposal aims to involve all these groups in a cooperative effort.

Much like the people whom it seeks to understand, autism research is prone to a sort of "weak central coherence": with a multiplicity of hypotheses targeted at particular systems or levels of analysis, the most vexing problem often is not identifying the observational details, but assembling these details into a single, coherent theory. The tragedy of autism research is that its work has been fractionated within many separate models of dysfunction, reflecting the many separate perspectives and approaches of cognitive neuroscience that have been brought to bear on it. These models only now are beginning to be combined. Focusing on autism's social deficits, some have characterised autism as a dysfunction in a cognitive module for "theory of mind," the ability to think in terms of social partners' beliefs and desires (Baron-Cohen et al. 1985, 2002). Others explain both social and non-social phenomena as consequences of a more general dysfunction of executive control (Hill 2004), shifting and distribution of attention (Allen & Courchesne 2001), "central coherence" of gestalt or global-level percepts (Frith & Happé 1994; Happé & Frith 2006), or an enhancement of local processing often at the expense of engaging intact global-level processing (Mottron et al. 2006). Though each of these theories seems to contain at least a piece of the picture, the process of putting these pieces together has begun only recently (Belmonte et al. 2004b; Mottron et al. 2006).

In science as in any human endeavour, what is discovered is constrained by what is looked for. All too often, experiments are framed so as to confirm or to refute hypotheses within one theoretical framework. "Theory of mind" studies show deficits in tasks of attributing false belief (Baron-Cohen et al. 1985), executive function studies show deficits in tasks of planning (Hughes et al. 1994) and inhibition of prepotent responses (Ozonoff et al. 1994), attention studies show slowed shifting (Courchesne et al. 1994) and abnormal distribution (Townsend & Courchesne 1994; Burack 1994) of attention, studies of central coherence show facilitation on tasks of perceptual disembedding (Shah & Frith 1994; Plaisted et al. 1998), and perceptual studies show enhanced discrimination of first-order stimuli (Plaisted et al. 2003; Bertone et al. 2003, 2005). Each of these foundational results has been individually confirmed by further explorations, but each has remained largely unintegrated with other findings.

Significantly, within each of these domains of exploration there is very appreciable variance in behavioural and physiological measures: many children with autism pass tasks of first-order or even second-order belief attribution (Frith & Happé 1994), deficits in executive function vary across task paradigms, executive subdomains, and individuals (Hill 2004), attention varies between abnormally narrow 'spotlight' and abnormally broad distributions (Townsend & Courchesne 1994), central coherence as measured by the Embedded Figures Test varies substantially within the autism population and in fact correlates with similarly variable performance on "theory of mind" tests (Jarrold et al. 2000), and perceptual variation in motion coherence thresholds is very large with a third of the autism population within the normal range (Milne et al. 2002; Belmonte 2005). Despite this richness of variance within perceptual and cognitive domains, with a few notable exceptions (e.g. Jarrold et al. 2000) the covariance structure between domains remains unexplored. Linking these investigations is important because in illuminating pervasive abnormalities of neural information processing that span cognitive domains, it can explain how these domains normally relate to one another computationally and developmentally.

Recent theoretical constructions of autism have converged on the notion of a systems-level dysfunction in neural computation (Belmonte et al. 2004ab), one whose interactions with normal programmes of brain and cognitive development may result in perturbations at many levels of processing. Autistic deficits in complex social and communicative skills are comparatively well studied, since these deficits are the most obvious, the most diagnostic, and the most debilitating. However, the relevance of abnormalities at lower levels of function (Rogers & Ozonoff 2005) ought not to be ignored, as perturbations at these simpler, more tractable levels of processing may offer insights at the systems level. In particular, correlation between behavioural and physiological studies of sensory and attentional phenomena on the one hand, and complex social cognitive processes on the other, may illuminate abnormal modes of development in which a systems-level abnormality perturbs both low and high levels of processing, and/or abnormal developmental cascades in which dysfunction at low levels of processing perturbs activity-dependent development at higher levels. Support for the notion of such multi-level cascades of perturbed development comes from the success of interventions addressing rapid auditory sequence processing in language and communication disorders (Tallal et al. 1996, 2004; Fitch & Tallal 2003), from studies of schizophrenia demonstrating deficits in early sensory processing (Butler & Javitt 2005; Uhlhaas & Silverstein 2005; Butler et al. 2007) and relating auditory frequency discrimination to deficits in affect recognition (Leitman et al. 2007) and visual size discrimination to deficits in theory-of-mind (Uhlhaas et al. 2006), from physiological studies of autism suggesting compensatory processing for dysfunctions in early sensory and attentional computations (Belmonte & Yurgelun-Todd 2003) and behavioural studies linking joint attention to theory-of-mind and pretence (Charman 1997), and even from studies of normal development and ageing showing that deficits in automatic, early processing evoke downstream, compensatory abnormalities in later, more effortful stages of neuro-cognitive processing (Townsend et al. 2006). In each of these instances, what seems on face an alteration of higher-order cognition is seen to be related to, and in some cases a consequence of, perturbations at lower levels of processing. Though such relationships may be most obvious in cases of clinical disorders, they seem unlikely to be limited to disordered cognition and instead may extend to normal variation.

1.2 The Importance of the Network Level

During the past decade, the neurobiological study of neuropsychiatric disorders has benefited from a new focus on connectivity between brain regions (Frith 2003; Fusar-Poli & Broome 2006). In particular, the systems-level dysfunction in autism has been characterised as a network dysfunction possibly comprising abnormally strong and undifferentiated connectivity within local networks and a resultant failure to develop normal patterns of long-range connectivity amongst brain regions and amongst cognitive subsystems (Brock et al. 2002; Belmonte et al. 2004a; Courchesne & Pierce 2005). This idea is consistent with an emerging collage of autism suscpetibility genes that perturb neural connectivity by altering neurone numbers, synaptic structure, or neurotransmission (Belmonte & Bourgeron 2006) – many of which may be responsible for dimensions of normal as well as abnormal cognitive variation (Ronald et al. 2006ab) – and has been supported by functional imaging results in autism demonstrating abnormally strong activation within brain regions that subserve low levels of processing along with abnormally weak activation within higher-order, integrative regions (Belmonte & Yurgelun-Todd 2003), and abnormally weak functional connectivity between brain regions (Just et al. 2004; Belmonte et al. 2008a), as well as by anatomical studies of high local and low bridging white matter volume (Herbert et al. 2004) and low diffusion anisotropy in white-matter regions subserving integrative processing (Barnea-Goraly et al. 2004).

The recency of interest in neural connectivity in autism arises in the context of neuroscience's historical focus on single-variable problems. Science as a matter of course directs its enquiries towards well framed and tractable hypotheses in which one independent variable is manipulated whilst all other factors are somehow held constant. Historically, this single-variable focus has produced great advances in the understanding of the effects of brain lesions (in which a single anatomical structure is silenced) and single-gene disorders (in which one gene is silenced or gains function). Complex neuropsychiatric conditions, though, are anything but single-variable problems. In autism in particular, the one truth that has become clear from decades of study is that this behaviourally defined condition converges from many possible ætiological factors and combinations thereof, and diverges into a welter of endophenotypic variability (Belmonte et al. 2004b). The lesion model is as poor a one as the single-gene model for understanding developmental disorders, since the experience-expectant maturation of any one brain structure depends on its receiving properly patterned inputs from the structures with which it communicates, and thus a perturbation of any one region becomes a perturbation of the entire network of interacting brain regions (Johnson et al. 2002), just as variants in a collection of genes combine to produce emergent variation in networks of interacting genes (Belmonte & Bourgeron 2006).

1.3 Applying 21st-Century EEG Hardware and Analytical Methods

Despite its crucial role in generating this hypothesis of abnormal connectivity, fMRI is of only partial use in testing it because its low temporal resolution misses out high-frequency phenomena that evolve over brief temporal intervals. Electroencephalography (EEG), on the other hand, can quantify brain connectivity within processes operating on millisecond time scales, has been central to the study of attention and perceptual organisation (Tallon-Baudry & Bertrand 1999), and has been suggested as a method of investigating a physiological basis for weak central coherence in autistic perception (Brock et al. 2002). The time is particularly ripe for renewed EEG studies of autism not only because of EEG's strong relevance to this question of neural connectivity, but also because of this past decade's developments in EEG acquisition hardware and multivariate and time-frequency EEG analytical methods, and because of the groundwork laid by previous EEG studies of autism – studies whose tantalising results demand and deserve replication and re-interpretation in the context of updated methods and theories. Unencumbered by the severe and restrictive conditions of fMRI (need to remain perfectly still, confinement to the magnet bore) or MEG (need to remain very still), EEG maximises subjects' freedom while providing exquisite temporal resolution, and increasingly precise spatial resolution.

A new generation of EEG amplifiers capable of matching much higher scalp impedances (Ferree et al. 2001), combined with sensor webs that parallellise the process of electrode placement and electrolyte application, has significantly reduced electrode application time and demands for subject compliance, enabling high-density EEG recording in a wider range of patients. Even more significantly, during the past decade as biologists have begun to communicate better with physicists and mathematicians, outdated univariate methods of analysis in the time domain have been supplanted by multivariate methods such as Independent Components Analysis (Bell & Sejnowski 1995) and by time-frequency analyses that account not only for signals phase-locked to stimulus or response events but also for signals consisting of perturbations of ongoing oscillations (Makeig et al. 2002, 2004). These advanced analytical methods have now been made available in a well documented and functional software package, EEGLAB (Delorme & Makeig 2004), which largely automates their application. Despite the availability of these techniques, though, most EEG studies still apply twentieth-century strategies of time-domain averaging at just a few electrode sites, ignoring frequency-domain measures such as non-phase-locked spectral perturbations and actually discarding most of the data available from high-density electrode montages. The current project is an opportunity to help train a new generation of students who will be conversant in this intersection of neurobiology and applied mathematics, and to explore normal and abnormal brain dynamics using these 21st-century methods.

Quantitative time-frequency analysis also opens EEG studies to measurement of temporally extended events, to which brain electrical responses may not be precisely time-locked. Even when the precise timing of an event within a blocked condition is unknown, EEG power and EEG coherence within specific frequency bands, and activity within and transient coherence between specific neural generators (i.e. specific independent components), can be assayed in a blocked rather than an event-related comparison. This method offers the opportunity to apply EEG's high frequency sensitivity to brain responses arising during comprehension of extended narrative sequences and other complex stimuli particularly relevant to social cognition.

EEG was one of the first neurophysiological recording methods applied to autism, and the source of several provocative results including the reduction or absence of several frontal event-related potential (ERP) components related to selective attention (Ciesielski et al. 1990; Courchesne et al. 1994), variability of attention-related ERP responses to sensory events (Lincoln et al. 1993; Kemner et al. 1994), and a lack of attentional modulation of sensory ERPs (Buchwald et al. 1992; Townsend & Courchesne 1994; Lincoln et al. 1995) – all of which collectively suggest an absence of modulation of distributed neural systems in response to task context. As autism research expanded over the past decade, though, EEG investigations did not expand as rapidly as MRI-based techniques. Especially in light of current ideas on abnormal neural coupling and dynamics in the autistic brain, many findings from past research on autism call out for replication and extension in ways not amenable to the low-temporal-frequency sampling of functional MRI. Event-related potentials and behavioural studies of motion perception, for instance, have never been combined within the same set of subjects. The very first studies of γ EEG response during perceptual binding in autism (Grice et al. 2001; Brown et al. 2005) find increases in induced γ power consistent with a hypothesis of abnormally weak neural inhibition within regions and abnormally low coherence between regions, and replication and extension of these findings is important. A deficit in γ synchrony, a putative mechanism for perceptual binding (Tallon-Baudry & Bertrand 1999), has been proposed as a mechanism for weak perceptual coherence (Brock et al. 2002), and initial studies of γ coherence in autism during a delayed match-to-sample task (Belmonte et al. 2004a) suggest abnormally strong frontal γ power but abnormally weak fronto-posterior γ synchrony. As this group has observed in the context of brain imaging (Belmonte et al. 2008b), understanding how autistic development plays out from genetic and environmental antecedents through many levels of brain structure and function demands correlative work. The proposed combination of tasks ranging in complexity from sensory and attentional to social cognitive would build such correlative knowledge within the sphere of electrophysiology, laying a foundation for future, even more broadly integrative studies that would include other measures of phenotype and genotype.

In addition to new data on autism, the proposed study would produce new normative data on the generators of event-related potentials, which historically have been characterised in terms of their latencies and their distributions over the scalp – parameters whose relation to independent brain electrical generators is only appproximate. Especially at long latencies, by which time activations have spread throughout large, distributed networks, these well characterised ERP components are liable to be superpositions of spatially blurred fields from multiple generators. The process of dissecting these superpositions into their constituent independent components has only just begun (Makeig et al. 2004), and further normative data will be a significant contribution.

1.4 Achieving Ecological Validity with Games

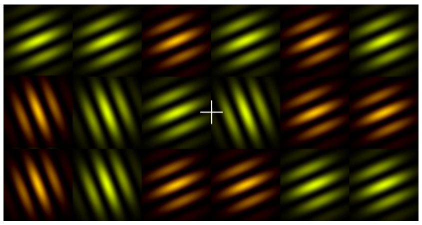
Perhaps the single most important obstacle to integrative studies is the practical limit on the amount of time that a single experimental subject (especially one from a clinical population) can reasonably be expected to perform before becoming fatigued. Unfortunately, often the more controlled a stimulus is from the scientist's point of view, the more repetitive and tedious the experiment can seem from the subject's point of view. Behavioural research on autism in recent years has highlighted the importance of motivation, behavioural set, and task instruction in establishing cognitive strategy and determining performance (e.g. Plaisted et al. 1999; Dalton et al. 2005). In light of these considerations, we have embedded experimental stimuli in the context of a video game that captures and maintains subjects' interest, transparently collecting behavioural data and synchronising with physiological recording as the subject plays the game. The practical advantages of such an engaging and ecologically valid format over the usual repetitive blocks of trials are legion. Indeed, varying levels and demands of attentional shifting and multimodal integration are natural in the context of video game play, and psychophysical measures such as dot motion coherence and embedded figures are easily implemented as, for example, the movement of a star field on a view screen and the detection of an object in a cluttered environment. In addition, the strategic and adversarial nature of a video game carries natural opportunities to explore higher-level cognitive measures such as comprehension of game-related narratives and social attribution to a computer-generated adversary. Video games evoke measurable alterations in attention and perceptual processes (Green & Bavelier 2003, 2006ab, 2007; Castel et al. 2005; Feng et al. 2007), and the video game format is increasingly being used to acquire simultaneous behavioural and EEG observations in ecologically valid contexts, for example in visuomotor tracking (Smith et al. 1999), air traffic control (Brookings et al. 1996), and military command and control simulations (St John et al. 2002, 2004; Berka et al. 2004). Recent results in human-computer interaction (von Ahn 2006) also point to the power of the game context to establish and to maintain motivation in tasks that otherwise might not seem engaging, and to teach persons with developmental disorders (Golan & Baron-Cohen 2006). Also along these lines, the video game format affords subjects more of a chance to become comfortable with the task before entering the laboratory, minimising the potential confound of state anxiety associated with performance of an unfamiliar task in a testing situation.

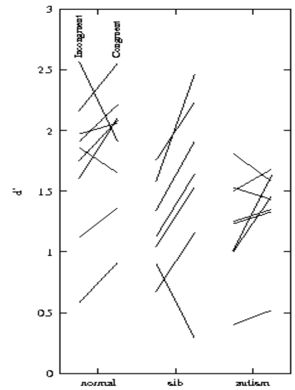
1.5 Contrasting Sibs to Highlight Critical Developmental Differences

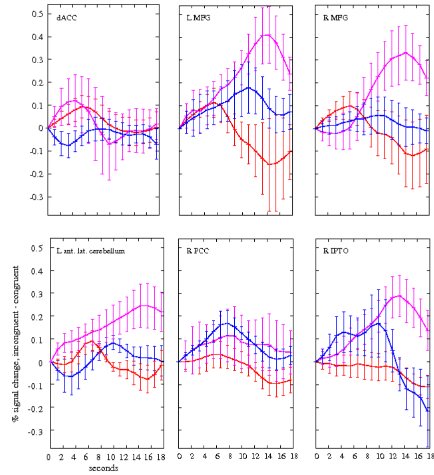
There is a significant genetic component to neuropsychiatric disorders in general, and autism is one of the most strongly heritable of these (reviewed in Belmonte et al. 2004b, and Belmonte & Bourgeron 2006); autism's sibling recurrence risk is over twenty times its incidence in the general population. Developmental disorders may well arise when an accumulation of liability factors interacts to perturb a developmental course permissive of the disorder into one determinative of the disorder. Information on the abnormal events surrounding this critical developmental event becomes much more valuable when it can be contrasted with information on what happens when the event is avoided. Such a contrast can be obtained by studying siblings and other family members of people with autism, people who presumably share some of the genetic susceptibility factors but in whom those factors have not become magnified into the full syndrome of autism. A wealth of behavioural data (reviewed in Belmonte et al. 2004b) suggests that such factors are operative in first-degree relatives and do produce subclinical abnormalities, including impairments of social cognition and superiorities on tasks of perceptual disembedding. In recent years these subclinical familial traits have been recognised in the Broader Autism Phenotype (Piven et al. 1997; Dawson et al. 2002). The first functional imaging studies of autism siblings (Dalton et al. 2007) have begun to add a physiological dimension to this similarity. This group's own fMRI work (Belmonte et al. 2008a), in a visual attention task involving suppression of incongruent distractors, suggests that delayed and prolonged fronto-cerebellar activation found in autism probands and in clinically unaffected siblings reflects familial, permissive factors, whereas a decrease in functional connectivity between brain regions is found only in probands and reflects more determinative factors. An understanding of how it is that some family members become autistic whilst others escape autism will further the understanding of normal development, and may help open the door to targeted interventions that may block this evolution from liability to disorder. In our view, the best possible outcome of such efforts would be a world in which the unique perceptual strengths that arise in people with autism and their family members are preserved, but combined with intact communicative abilities that will give these individuals a chance to interact with the surrounding social world and to share their unique gifts.

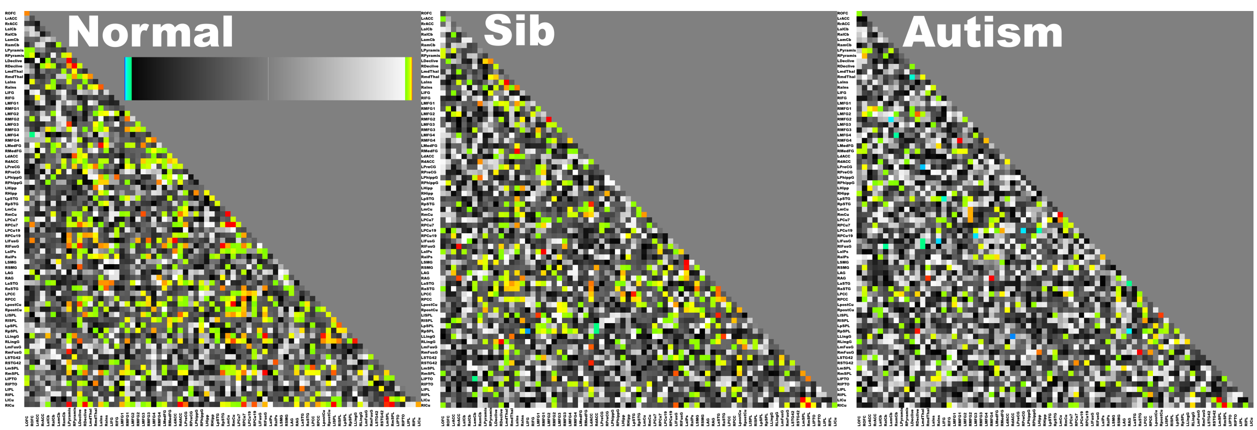
1.6 Preliminary Results As a motivation for the proposed correlational analyses across cognitive domains, behavioural and physiological data are presented from recent work within the domain of visual attention. As proof of principle, details from a prototype implementation of the game paradigm are also presented, along with an example application of the proposed EEG analysis strategies in the context of an attention experiment.

The visual attention study compared 8 10-to-15-year-old boys with autism spectrum conditions (diagnosed using the same procedure specified below for the proposed study), 7 clinically normal brothers of people with autism spectrum conditions, and 8 unrelated normal boys, with all groups matched for age, IQ, and handedness. The task was a visual divided-attention task within briefly (167 ms) presented stimulus arrays in which the congruence of spatially intervening distractors was varied (left figure below). Subjects had to report, via a forced-choice button-press response, the presence or absence of a conjunction of colour in one location and orientation in another. Both behavioural performance (d') and brain activation (BOLD time courses) were measured as a function of the level of distractor congruence. d' scores (middle figure) differed significantly by diagnosis ($F(2, 84) = 5.99$, $p=0.0037$), being lower than normal in the sib group ($t(62) = 2.36$, $p = 0.0217$), and lowest in the ASC group ($t(66) = 3.42$, $p = 0.0011$). This behavioural result establishes the practicality of differentiating samples even in such small groups, but by itself is not entirely surprising since previous results in social cognitive domains (discussed above) have already established that non-autistic sibs manifest an intermediate degree of the autism behavioural phenotype. The surprise comes in the physiological data (right, red=normal, blue=autism, magenta=sibs), which reveal a pattern of prefrontal and anterior lateral cerebellar activation in both the autism and sib groups that is prolonged far beyond the end of the trial, and which fails to peak and to resolve at the rapid rate characteristic of the normal group (comparisons significant in cerebellum and left middle frontal gyrus for autism versus controls). In fact, this delayed activation is even greater in the sib group than in the autism group (comparisons significant in cerebellum, bilateral middle frontal gyri, and right posterior intraparietal sulcus (area V7) for sibs versus controls), suggesting that it may reflect a process that compensates for an inefficiency in the rapid deployment of attention, and that this compensatory process is more completely implemented in the clinically unaffected family members. In contrast to this abnormality in the timing of fronto-cerebellar activation manifest both in the autism group and in clinically unaffected sibs, significant decreases in functional connectivity between brain regions were manifest only in the autism group, and differentiated this patient group both from the sibs and from the normal controls (bottom figure: coloured cells denote significant correlations in the correlation matrix; collapsing across all pairs drawn from 76 brain regions in this matrix, $F(2, 1821) = 266.89$ for the omnibus test and $t(1291) = 20.71$ between autism and normal, $t(1139) = 19.84$ between autism and sibs, but $t(1215) = 0.72$ between sibs and normal – the important message in the figure is the overall level of functional correlation, more than the specific pattern of regions involved). **Collectively, these results suggest that abnormal timing of attention-related activation within frontal and cerebellar regions is a familial trait <u>permissive</u> of autism, whereas abnormally low functional connectivity between brain regions may reflect processes more <u>determinative</u> of autism.** These findings fit well within a paradigm of interactive specialisation of cognitive function which underlies both normal and abnormal brain development. The natural follow-up question is how is this familial liability developmentally translated into the full syndrome of autism, and how might this maldevelopment be interfered with?



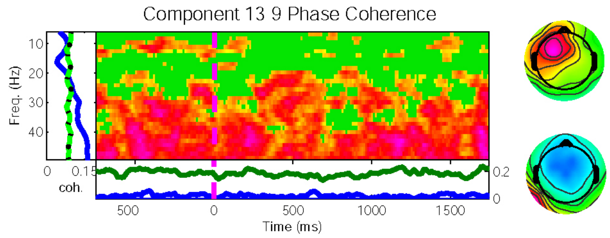






The details of the video game paradigm and software are described in more detail in the methods section below. In brief, the game is a collection of mini-games themed around the construction of a space colony: resources must be gathered in order to build the colony, and the colony must cooperate with friends and defend against adversaries as it collects these resources. This group has found that this sort of systematic project centred on themes of science fiction and technology is especially engaging for normal children, and also of interest to children with high-functioning autism. The current prototype includes a complete implementation of the first of these several mini-games and nearly complete drafts of two others, and also implements a core of shared subroutines for stimulus timing, behavioural data collection, and event logging. This game served as the senior project for two undergraduates in the Game Design Initiative, and was presented as part of the spring 2007 Game Design Showcase at Cornell. Both the student designers and their classmates were impressed with the degree to which the tight tolerances for timing and experimental control were in fact compatible with the implementation of an exciting game that children (and adults) want to play. In pilot work within the laboratory, this game has been successfully applied to measure motion coherence thresholds, and go/no-go accuracy and reaction time.

Data from a multimodal attention experiment serve to demonstrate the feasibility of the EEG analyses that we propose. The task was one of auditory-visual integration: subjects made a forced-choice response as to whether a picture matched a sound presented 0 to 250 ms later. The figure below shows sustained gamma EEG coherence (left plot) between auditory (top right scalp map) and visual (bottom right scalp map) components during the simultaneous condition. Even though components are in general independent, and are identified as such by Independent Components Analysis, cognitive manipulations induce transient coherence between these components, and this coherence serves as a measure of functional connectivity. Unlike channel-by-channel averaging, Independent Components Analysis makes use of all the data available from today's high-density electrode networks. The same analytical techniques and principles as have been applied in this study will be applied in the proposed work.



The proposed age range of 10 to 15 years is motivated by our results in previous work, and by results on the maturation of EEG and ERP measures. As a useful generalisation, age-related investigations of visual (Doucet et al. 2005; Pompe et al. 2006), auditory (Ponton et al. 2000; Bishop et al. 2007), and attentional (Mueller et al. 2008) event-related potentials have revealed ongoing change in peak amplitudes and latencies that begins to reach adult-like levels around the age of 10 years, with much of the maturation complete by the age of 13 years. This target range therefore affords an opportunity to capture these developmental changes by including age as a factor in the analyses. In addition, in this research group's experience the 10 to 15 age range is an ideal one for the level of task complexity involved in this video game paradigm.

1.7 Investigator Qualifications Belmonte's work for the past decade and a half has addressed the relation between normal and autistic development using techniques of quantitative EEG and fMRI, and has cut across subdisciplines and ideologies. His education and experience are wide-ranging and integrative: his postgraduate training took place in the laboratories of Eric Courchesne at UCSD, focusing on EEG, MRI morphometric, and behavioural studies of attention in autism, and Deborah Yurgelun-Todd at McLean Hospital, focusing on cognitive fMRI studies. His postdoctoral work was with Simon Baron-Cohen at Cambridge, combining his past experience in low-level studies of attention and perception with a new focus on methods of investigating high-level social cognition. During fall 2007 he was a visiting member of the Computational Biology and Bioinformatics Program at the Broad Institute at MIT, gaining experience in psychiatric genetics and computational genomics and collaborating with autism groups at Massachusetts General Hospital and the MIT Media Laboratory.

Initially educated as a computer scientist, Belmonte spent two years as a scientific programmer in the Movshon laboratory at the New York University Center for Neural Science, and this work made him familiar with practical details of software and hardware for the display of visual stimuli. In addition, Belmonte gained intensive experience in auditory psychophysics during his work in industry on computational models of the human auditory system (Schmidt & Belmonte 2004). (The stimuli in the perceptual portions of this proposal draw on these experiences.) He has expertise in nonparametric statistical methods for analysis of biophysical time series, having designed statistical programs for permutation testing of fMRI (Belmonte & Yurgelun-Todd 2001) and EEG data. His previous EEG work combined these nonparametric statistics with frequency-domain analyses to identify an effect of visual spatial attention on EEG phase-locking (Belmonte 1998, 2000). At Cornell, Belmonte maintains close links with the Faculty of Computing and Information Science and specifically with its Game Design Initiative.

Belmonte has a proven record of generating novel and productive collaborations. Much of his attention has been devoted to combining expertise and unifying subdisciplines: he is first author of several high-profile collaborative papers, on abnormal neural connectivity as a biological theme around which to unify disparate psychological theories (Belmonte et al. 2004b), physiological results (Belmonte et al. 2004a), and genetic findings (Belmonte & Bourgeron 2006), and most recently on how to overcome technical and social obstacles to collaboration and sharing of neuroimaging data (Belmonte et al. 2008b). In addition, as interim chair of the Publications Committee of the International Society for Autism Research in 2006, he played a key role in expediting organisation of the Society's new interdisciplinary journal.

1.8 Facilities and Resources Developmental cognitive neuroscience is a growing focus within the Department of Human Development's research and teaching portfolio. The department has expanded its commitment to this area with the construction of a new EEG laboratory containing a 128-channel BioSemi ActiveTwo system and a growing undergraduate involvement in cognitive neuroscience courses and research. The department has access to a research-dedicated 3-Tesla Siemens Trio MRI scanner and accompanying mock scanner at the Rochester Center for Brain Imaging. The department maintains close links with the local autism community, principally via the autism services programme at the Franziska Racker Centers in Ithaca. A centrepiece of the department's mission is outreach and practical dissemination of research results, both via affiliations such as the Racker Centers and via Cornell Cooperative Extension.

The Game Design Initiative at Cornell (GDIAC), headed by Walker White, is an interdisciplinary group incorporating computer programmers, artists and designers working cooperatively to transform game concepts into professional-quality video game software. GDIAC supports undergraduate courses in game design and development, game-orientated graduate student projects, a youth outreach programme, and interdisciplinary and collaborative undergraduate research in a wide range of departments and disciplines from economics to fine arts. GDIAC has implemented a multidisciplinary curriculum on the theory and application of video game design including artificial intelligence, network programming, physics, art, music, neuroscience, media studies, and technology and society.

2. SPECIFIC OBJECTIVES

1. As part of the undergraduate practicum in the Game Design Initiative at Cornell, continue the ongoing development of freely available, open-source, extensible software that encapsulates a battery of perceptual, attentional, and social cognitive tasks in a video-game format suitable for behavioural and physiological measures. Experimental paradigms are valuable insofar as the timing and other parameters of their stimuli are well specified and controlled, and insofar as they yield data relevant to the cognitive processing that occurs under ecologically valid conditions. These two goals often are at odds, since well controlled stimuli often are too repetitive to sustain subjects' motivation. A growing body of literature demonstrates that video games may provide a way between the horns of this dilemma. This group's pilot project with the Game Design Initiative at Cornell has demonstrated the feasibility of embedding well controlled stimuli and behavioural responses in the context of an engaging video game, which the proposed project will continue to refine and to integrate with student projects.

2. Use behavioural and EEG data to correlate phenotypic measures in this range of tasks in a population of 10-to-15-year-old children with autism spectrum conditions (ASC), and contrast these measures with normal controls. Using these same measures, contrast phenotypes in 10-to-15-year-old clinically unaffected sibs of people with ASC with those in ASC and in normal controls. Although cognitive neuroscience has produced many studies within each of these task domains in contexts of both normal and disordered development, correlative studies exploring the covariance structure across domains have been less common. Results on clinical disorders suggest that higher-order cognitive abnormalities may relate to, or even arise from, perturbations at lower levels of processing. The theory of interactive specialisation suggests that such developmental relationships between cognitive subsystems are not limited to clinical disorders but play an important part in normal cognitive development, and leads to the hypothesis that measures in these domains will correlate not only in the case of disordered development but also in the case of normal cognitive variation. Behavioural and physiological examination of these three subject groups will address this central hypothesis.

3. Share all stimuli and and analytical methods with other investigators to facilitate future expansion of behavioural and EEG data acquisition to a multi-site population. Facilitate future data mining and discovery by sharing all data (EEG, structural MRI, behavioural, diagnostic, and psychometric) collected during these experiments, in anonymised form, via an online data resource accessible via the World Wide Web by the entire autism research community. Share results and practical implications with central New York's autism community via public forums and presentations. Understanding how neural systems connect and communicate demands that scientists themselves communicate, both with each other and with the public whom they serve. Every resource developed in the course of this project – methods, tools, and data – will be made freely available to the scientific community. In addition, people with autism spectrum conditions and their families and educators will be involved as part of outreach efforts, a major focus of Cornell's College of Human Ecology.

3. METHODS AND PROCEDURES

3.1 Methods for Objective 1 (software development): The video game is in the final stages of development as a joint project with the Game Design Initiative at the Cornell University Faculty of Computing and Information Science, with an initial release scheduled for fall 2008. The game is written for the widely used Microsoft Windows operating system, using the XNA Game Studio Express SDK and the Visual Studio Express integrated development environment available at no cost from Microsoft. High-resolution timing and display synchronisation within the game ensure millisecond accuracy of the event timing. All game events (stimulus onsets, key presses, &c.) are logged to a plain text file which can be transmitted to a central server for offline analysis. Events also are sent as byte codes to a parallel port for synchronisation with EEG acquisition. The game is organised as an extensible collection of mini-games built around a main game, and documentation is provided for programmers who wish to add new mini-games that will make use of a core collection of subroutines for display manipulation, event logging, and psychophysical parameter estimation. The main game involves the player in the design and construction of a space colony, and shares thematic elements with other simulation-building games such as SimCity which, as industry experience shows, appeal equally to players of either gender and of a broad range of ages. In order to construct and to maintain the city, players must enter the mini-games in order to collect resources and to defend against hazards. In addition to supplying a thematic framework around which the mini-games are unified, the strategic element of this core game provides an opportunity to evaluate cognitive planning in a fairly open context. The main experimental measures, though, are built into the mini-games.

The “Meteors” mini-game resembles the arcade games Tempest and Asteroids, and combines tests of motion coherence threshold, motor inhibition, and executive flexibility. The player commands a spaceship that moves clockwise (right arrow key) or counterclockwise (left arrow key) around the perimeter of a circular field. Slow-moving meteors materialise at the centre of the field and drift outward; the player must fire torpedoes (space bar) to destroy these meteors. (This ongoing task serves simply to maintain vigilance.) Periodically, a wormhole materialises within the field. The player can open this wormhole by moving around the circle to align with it, then connecting with the wormhole (up arrow). Connecting temporarily drains the ship's propulsion systems; the ship is locked in place in front of the wormhole as an unidentified ship begins to emerge. This ship can be either a friend or a foe, with equal probability. Friend and foe ships are identical in area and luminance, but differ subtly in form: one has two warp nacelles protruding, the other three. Firing on a foe prevents the foe from firing on the player and weakening the player's shields. Conversely, withholding fire on a friend is rewarded by a weapons power-up which increases the player's firing rate. (This change in firing rate alters the game tactically but does not affect measurement of reaction times.) Friends and foes cannot be discriminated until they have emerged from the wormhole. Thus during the opening of the wormhole the player must prepare, but not execute, a motor response. Foes do not fire, and friends do not deliver weapons power-ups, until 800 ms after emerging. A hit in this task is therefore defined as firing on a foe within this 800 ms interval, a miss as failing to fire on a foe within this interval, a correct rejection as withholding fire on a friend, and a false alarm as firing on a friend. This task behaviourally measures inhibitory function, and can be used in conjunction with EEG measures to assess motor planning.

Friendly and enemy forces have no fleets of their own, but instead commandeer one of two classes of ships. The class of ship used by each side therefore can change from one session of the game to the next. A shift session is one in which the assignment of ship classes differs from that of the session immediately preceding. A hold session is one in which the assignment of ship classes does not differ from that of a session immediately preceding. Differences in reaction time and accuracy for the fire-or-withhold task between shift and hold sessions measure executive flexibility.

After the player has completed a session of five wormhole connections, the ship warps to another meteor field. Whilst in warp, the player views a field of 200 stars (white dots on a black background), a percentage of which move coherently in one direction, either left or right. Other stars move in random directions. Each star appears in the field for four video frames, or until its motion carries it outside the boundary of the field. Coherent motion of the star field signals that the ship is veering right (for leftwards apparent motion) or left (for rightwards apparent motion) of its intended course. The player's task is to compensate for this drift by steering left (left arrow) when leftwards apparent motion is perceived, and right (right arrow) when rightwards apparent motion is perceived. Compensating for drift saves fuel. Failure to compensate for an actual drift costs fuel, as does compensating when no drift is present. Each drift interval lasts 2 seconds plus a random and uniformly distributed interval between 0 and 250 ms, or until a course correction is commanded. The player's motion coherence threshold is estimated via parameter estimation by sequential testing (Pentland 1980; Lieberman & Pentland 1982).

The “Ore Factory” game tests distribution and shifting of attention, and the effect of multimodal (auditory and visual) stimuli. The player fixates on a base at the bottom centre of the display, where (s)he performs a standard “oddball” task of sorting good ore from contaminated (coloured) ore to be used as a raw material for the space colony. Concurrently, valuable bonus resources materialise in the periphery, spatially and temporally interspersed with valueless distractors. The periphery is divided into four sectors, and at any given time a spatial cue indicates exactly one of these sectors as the most likely location in which bonuses may appear. A pattern of background interference in the sensors flashes at a fixed frequency within each sector, thus allowing covert attention to each sector to be encoded as the amplitude of a steady-state evoked potential at the corresponding frequency – a technique with which this group has experience (Belmonte 1998, 2000). In three phases, the game tests the spread of visual spatial attention around a covertly attended sector (Townend & Courchesne 1994), implements a Posner-style test of valid and invalid cueing during shifts of attention from one sector to another (Posner et al. 1987), evaluates the effect of distractors on performance in the peripheral task (Burack 1994), and compares multimodal versus unimodal cueing (Molholm et al. 2002).

The "Signals Intelligence" game includes both a test of perceptual disembedding and an adaptation of the classic "Sally Anne" test of theory-of-mind. In the "Sally Anne" test one character, Sally, places a marble in a safe place, and then whilst Sally is out of the room another character, Anne, moves the marble to a new hiding place. The subject is asked "Where will Sally look for her marble?" or "Where does Sally think the marble is?" Many autistic children, like normal children under four years of age, answer this question erroneously in terms of what they themselves know about where Anne moved the marble, instead of what Sally knows. Those who correctly answer this first-order theory-of-mind question may still respond incorrectly to a second-order question: if, unbeknownst to Anne, Sally was peering through the keyhole and saw Anne move the marble, "Where does Anne think Sally will look for the marble?"

The player moves through an alien laboratory to reach communications terminals. On reaching a terminal, the player can "hack" the communications system by picking out embedded figures from a "Matrix"-like stream of graphics. This part of the game implements the Embedded Figures Test (Witkin 1950). Having hacked the communications system, the player gains decryption keys and becomes privy to a series of subspace transmissions, each of which is a brief animation. In animation #1, a friendly ship deposits a resource (e.g. fuel or materials) in a depot on one of several available planets. (Planets are readily distinguishable by their location on the star map and by their surface appearance.) In animation #2, an opponent ship appears and either steals the resource and deposits it on another planet (THEFT, $^{2}/_{3}$ probability) or simply scans the resource (¬THEFT, $^{1}/_{3}$ probability). Animation #3 is a picture of the friendly ship's control centre including its captain and its viewscreen, which shows either a sensor scan of the opponent's actions (SCAN, ½ probability) or noise representing sensor jamming (¬SCAN, ½ probability). Thus by the end of animation #3, one of three equiprobable situations exists: (1) the friend believes correctly that the resource is in its original location, and the opponent believes correctly that the friend will look for the resource in this location (¬THEFT); (2) the friend believes incorrectly that the resource is in its original location, and the opponent believes correctly that the friend will look for the resource in its original location (THEFT∧¬SCAN); (3) the friend believes correctly that the resource is in its new location, and the opponent believes incorrectly that the friend will look for the resource in its original location (THEFT∧SCAN). Animation #4 reminds the player that the friend will always set course to retrieve the resource, and that the opponent will always set course to intercept the friend. After this fourth animation, the player is prompted pictorially to lay in two intercept courses (by moving the mouse to the appropriate planet), one to rendez-vous with the friend and one to engage the opponent. In order to set these courses the player must infer where the friend thinks the resource is and where the opponent thinks the friend will look for the resource, respectively. Accuracy and response time in these tasks measure first-order and second-order theory-of-mind processing.

In order to avoid confounds with verbal ability (*e.g.* Peterson & Siegal 1999) as much as possible, all game instructions (for example, the assignment of friend and foe ship classes) are given as pictures and animations, and players are prompted to practise key-press responses in the appropriate game contexts. The instruction period provides a further opportunity to measure brain response to these pictorially presented narratives.

The project's structure as a collection of mini-games lends itself to parallel but collaborative efforts within small teams of designers and programmers, with each team focused on one or a few mini-games. As this format is extensible, it is anticipated that new games encapsulating new experiments will be added throughout the entire term of the project, providing a continuing series of instructional opportunities. The pedagogic impact of these game design projects will be evaluated over the course of each academic year, as undergraduates in each team present and defend their designs in Computer and Information Science 400, Advanced Projects in Game Design. Completed projects will be demonstrated at end end of each academic term in a Game Design Showcase open to the public. Emphasis is placed not only on knowledge of computer programming and design, but on the ability to apply these skills in the context of a team project, and to communicate the results in written and oral presentations – skills of great value in the games industry and in computational work in general.

3.2 Methods for Objective 2 (behavioural and EEG comparisons of ASC, sibs, and normal controls):

Subjects 10 to 15 years old will be recruited through the Franziska Racker Centers in Ithaca and the Cornell University and Ithaca communities. Subject groups will consist of children with ASC, sibs of children with ASC, and unrelated normal children with no psychiatric or neurological history. Groups will be matched for age (individual matching to within 10%), Performance IQ (groupwise matching), sex and handedness (individual matching). As ASC is much more common in males than in females, and we wish to have sufficient data on both sexes in all three matched groups, recruitment will focus on enriching the ASC sample with females. For the specific video game paradigms cited in this proposal, sufficient numbers of subjects will be recruited in order for 32 subjects in each group to complete the study. It is anticipated that recruitment will continue in order to provide sufficient numbers for student projects (see below). **Inclusion criteria:** for ASC, a clinical DSM-IV-TR diagnosis of autism, Asperger syndrome, or PDD-NOS, not associated with any known comorbid genetic syndrome (*e.g.* Fragile X syndrome, neurofibromatosis, tuberous sclerosis, Rett syndrome, Angelman syndrome, Prader-Willi syndrome, Smith-Lemli-Opitz syndrome); for sibs, a brother or sister fulfilling the aforementioned ASC inclusion criteria but no autism-spectrum diagnosis in the sib themselves; for normal controls, no history of psychiatric or neurological disorder, and no family members with any history of developmental disorder; for all groups, no sensory deficit (*e.g.* blindess, colour blindness, deafness) that would interfere with game stimuli.

Diagnosis of ASC will be verified by administration of the Autism Diagnostic Inventory – Revised (Lord et al. 1994) and the Autism Diagnostic Observation Schedule – Generic (Lord et al. 2000) by a qualified rater (M.K.B. or a postdoc or graduate student who has received ADI-R and ADOS-G training). Traits of the Broader Autism Phenotype in the sib group will be assessed with the Broader Phenotype Autism Symptom Scale (Dawson et al. 2007) administered by a qualified rater (M.K.B. or a postdoc or graduate student who has received BPASS training).

Psychometric measures will be selected from the consensus recommendations of the Cure Autism Now Neuroimaging Summit (Belmonte et al. 2007), and will be carried out by undergraduate and postgraduate students under the supervision of the PI and postdoctoral staff. (The PI's laboratory includes a large number of undergraduates with training in psychological test administration.) In all subjects, IQ will be assessed with the Wechsler Abbreviated Scale of Intelligence (WASI), handedness with the Edinburgh Handedness Inventory, face recognition with the Benton Face Recognition Test, social perception with the Reading the Mind in the Eyes Test (Baron-Cohen et al. 2001), social communication with the Social Responsiveness Scale (Constantino et al. 2003) (completed by a teacher rather than a parent so as to avoid negative bias in sibs' ratings that might arise from parents' comparisons to their ASC children), and autistic or pseudo-autistic traits with the Autism Spectrum Quotient – adolescent version (Baron-Cohen et al. 2006). Subjects in the ASC group will be rated on the Repetitive Behavior Scale – Revised (Bodfish et al. 2000), with scores transformed and scaled according to the established factor loadings and variances for Ritualistic/Sameness Behavior, Self-injurious Behavior, Stereotypic Behavior, Compulsive Behavior, and Restricted Interests (Lam & Aman 2007), and on the Sensory Sensitivity Questionnaire (Minshew & Hobson 2008). As most of these measures are parent questionnaires that can be taken home and completed at leisure, the in-laboratory portion of the testing (WASI, Benton Faces, Eyes Test) can be completed in about an hour and a half, in one visit. This initial visit also will be used to familiarise the child with the experimental setting and the sights, sounds, and tasks of the video game.

As a complement to the senior personnel and graduate students and as an augmentation to the educational aspect of this proposal, undergraduate researchers will be recruited through the junior/senior-level course Human Development 474, Autism and the Development of Social Cognition, as well as through a departmental honours programme, and through the university's Rawlings Cornell Presidential Research Scholars programme which enrols distinguished freshmen and sophomores and provides research mentoring throughout the undergraduate years. Human Development 474 is an advanced undergraduate seminar that uses autism as a case study with which to approach general questions in developmental cognitive neuroscience, focusing especially on the contrast between theories of innate modularity and interactive specialisation. The seminar covers current psychological and neurobiological theories of autism, emphasising written analysis and critical review of the primary research literature. Specific topics are selected to match students' interests, and each student develops and orally defends a research proposal on an open question in the neuroscience of autism or related developmental disorders. The course stresses writing as a tool for thinking, and is designated as a writing-intensive subject; the instructor (M.K.B.) holds an advanced degree in writing and has experience teaching technical writing, and a postgraduate teaching assistant will receive training in writing instruction from Cornell's John S Knight Institute for Writing in the Disciplines.

Students will be given the option to tailor their research proposals for implementation within the video game format outlined here. As many of these proposals as can be accommodated will then become projects for students in the Game Design Initiative. Students thus will be able to see their own experimental paradigms brought to implementation, and will gain experience in working with scholars in other disciplines and managing their own research projects (under close supervision). After students have received training in the protection of human subjects, projects will culminate in the collection of behavioural and/or physiological data on young adult volunteers from the Psychology Department subject pool, and then on a subsample of the subjects recruited for the main video game experiments. Write-up and presentation of students' work will be presented in Cornell's intramural undergraduate research exposition, and potentially in larger scientific meetings and journals. In the course of this work, students will have opportunities for practical training in EEG recording technology, EEG data analysis, and autism assessment and psychometric testing, according to their individual interests. Cornell's undergraduate curriculum is especially in need of this practical cognitive neuroscience component: with most human neurobiological research located on Cornell's medical campus in New York City, the number of cognitive neuroscience research opportunities for undergraduates on the Ithaca campus has not kept pace with a growing level of interest and demand.

Recent technological advances have made it possible to implement high-density EEG/ERP recordings (64 to 128 channels) rather quickly. EEG/ERP data provide temporal resolution nearly equal to real-time brain activity measurements. In the proposed studies, topographic aspects of the data will be complemented by individual structural details obtained from MRI. Information about the timing and loci of neurophysiological processes is critical to understanding their role in information processing. Timing, magnitude, and topography of the ERPs will be assessed in order to derive this information. The more advanced EEG/ERP analysis techniques proposed here are provided by the open-source EEGLAB toolbox. These tools allow examination of oscillatory brain activity in the frequency bands relevant to the study of neural binding during various integrative processes. These analyses involve further dissecting the non-averaged (single-trial) EEG data and averaged (ERP) peaks into functionally meaningful, distinct neural information sources and characterising those sources in terms of timing, scalp topography, spectral characteristics, and "cross-talk" with one another. For example, it is known that each averaged ERP peak reflects multiple distinct neural processes that overlap in time. Independent Component Analysis (ICA) techniques in EEGLAB allow separation of EEG and ERPs into simpler components that may reflect underlying brain processes (Makeig et al. 2002, 2004; Delorme et al. 2004). ICA can also selectively remove artefacts from EEG without loss of relevant data. This group has successfully applied this technique to biophysical time series data (*e.g.* Schmidt & Belmonte 2004).

Using a high-resolution EEG/ERP acquisition system, Biosemi ActiveTwo, 128 channels of electroencephalographic (EEG) recordings will be obtained using tin electrodes distributed evenly across the scalp according to the modified International 10-20 System. By amplifying the EEG signal directly at the head, BioSemi's active-electrode technology eliminates amplification of inductive artefacts caused by head and body movements. Placing active electronics within millimetres of the actual electrode contact allows much greater impedances at the scalp-electrode interface, virtually eliminating the need to clean and to abrade the scalp before applying electrodes. Capping time is thereby reduced to less than 20 minutes for 128 channels, helping to ensure that the subject is not fatigued before the experiment begins. EEG recording will be performed by graduate student and postdoctoral personnel experienced with autistic children, under the PI's supervision. Undergraduate researchers will have the opportunity to assist; we are fortunate enough to have some highly skilled undergraduates, who can achieve capping times comparable to those of the PI and graduate students.

Eye movement artefacts (blinks and saccades) will be recorded by vertical and horizontal EOG electrodes. In addition, more stable recordings of eye position will be taken using an SR Research EyeLink 1000 infrared eye tracker. During the past months we have developed a close relationship with SR Research; their engineers have modified their gaze tracker to keep the power supply outside our shielded EEG recording chamber, and have even offered us the use of an ultra-low-noise version of the EyeLink that is under development for MRI-compatible applications. In our pilot work, the operation of the EyeLink tracker has added no noticeable degradation to our active-electrode EEG recordings.

EEG will be amplified using a bandpass of .01 to 200 hz, then digitised online at a rate of 512 samples per second. Movement artefact will be excluded manually from the continuous EEG data. Resulting EEG will contain repetitive, consistent eye movement and muscle artefacts which will be separated from brain activity using ICA (see above). Only the resulting artefactual ICA components (e.g., blinks, saccades, and muscle tension activity) will be removed from the EEG, leaving the rest of the data artefact-free for further analyses. Following artefact correction, averages of EEG activity will be made for each stimulus type (i.e. attended/unattended) for each subject in each test condition. Peak amplitudes and latencies will be extracted automatically within the following specified latency windows for components of special interest: P1 (most + in 80-130 ms), N1 (most – in 110-180 ms), P2 (most + in 130-240 ms), N2 (most – in 200-300 ms), P3a (most + 240-300 ms, frontal localisation), P3b (most + in 300-500 ms, parietal localisation). In addition, ICA will be applied to analyse continuous EEG decompositions to determine major cortical contributors to frequency bands of interest (e.g. θ (5-7 hz), α (8-12 hz), μ (motor-related activity in the α range)), β (13-30 hz), low γ (30-70 hz), and high γ (70-120 hz). Scalp maps of components derived from these decompositions generally point to compact cortical generators. Power, coherence and scalp distribution will be computed using EEGLAB, and dipole sources will be modelled using EEGLAB's DIPFIT routine. To facilitate source localisation of independent components and to bank data for future analyses of morphometry and anatomical connectivity, after successful acquisition of EEG subjects will be imaged in slices parallel to the AC-PC plane using a 1mm 3D MPRAGE sequence, a double-echo fast spin echo sequence, and a brief DTI sequence, on a 3 Tesla Siemens Trio system at the Rochester Center for Brain Imaging.

This study's predictions are motivated by this group's and others' contributions to the altered-connectivity theory of autism, by previous findings within individual experimental paradigms, and by the notion that interactive specialisation during development will produce cross-domain correlations not only in the case of the patient group but also in the case of the sibling and unrelated normal groups. (Specific predictions presented here are necessarily summarised and abbreviated because of the large number of tasks and analyses occasioned within the video game.) Within-domain findings and cross-domain correlations for the ASC group are expected to be largest in magnitude, and predictions for this subject group are presented first:

On the “Meteors” task, though results on inhibitory function in autism have differed across experimental paradigms (Hill et al. 2004), the execution of a response is expected to be prepotent (reflecting the high cost of a player's being destroyed versus the lesser benefit of receiving a power-up) and an increase in errors of commission in the ASC group is therefore expected, especially on the first trials of shift sessions in comparison to the first trials of hold sessions, reflecting deficits in inhibition of prepotent responses and in executive flexibility (Ozonoff et al. 1994). It is expected that the current results will replicate those of elevated motion coherence thresholds (Spencer et al. 2000; Milne et al. 2002; Bertone et al. 2003; Pellicano et al. 2005) and also will find that the normal induced γ EEG synchrony related to coherent motion (Müller et al. 1997) is reduced in ASC, reflecting disordered long-range functional connectivity. Reductions in the amplitude of the motor readiness potential (Rinehart et al. 2006) also are expected. On the peripheral targets in the “Ore Factory” task, the expectation is a group-by-distractors effect with the ASC group faster than normal in the non-distractor condition (O'Riordan et al. 2001) but slower in the distractor condition (Burack 1994), and in the cueing paradigm the expectation is a group-by-validity-by-SOA effect with slowed shifting of attention in ASC heightening the validity effect at 800 ms relative to 100 ms (Townsend et al. 1996). In the multimodal comparison with ICA separation of EEG components, it is expected that the normal interactions of evoked responses to auditory and visual cues (Molholm et al. 2002; Senkowski et al.. 2007) will be reduced in ASC, and that shortening of reaction times for multimodal relative to unimodal cueing will be decreased or absent in ASC. In the peripheral task it is expected that attentional modulation of steady-state evoked potentials amplitudes will support refinement of the somewhat equivocal finding of either abnormally focused or abnormally distributed P1 response as a function of spatial location (Townsend & Courchesne 1994), and it is hypothesised that the overall effect will be one of abnormally strong focus. In the “Signals Intelligence” game, superior performance on the Embedded Figures task (Shah & Frith 1983) is expected, as well as a group-by-condition effect with longer behavioural response latencies in the ASC group for the first-order and especially the second-order theory-of-mind conditions, as suggested by previous results employing accuracy measures in theory-of-mind tasks (Baron-Cohen 1995).

In all these visuomotor tasks the altered-connectivity theory (Brock et al. 2002; Belmonte et al. 2004a; Courchesne & Pierce 2005) predicts a reduction in the normally occurring (Frund et al. 2007) γ coherence between frontocentral and occipitoparietal component generators, and an increase in local γ power within generators. In the case of sibs, on the basis of this group's recent results (Belmonte et al. 2008) the predictions are behavioural performance between ASC and normal levels, frontal evoked potentials and local γ power increases resembling those of autism, but sparing of γ coherence. These are group predictions, of course; it is fully anticipated that there will be a great deal of within-groups variance on behavioural and physiological measures – and this variance is in fact what's being counted on, since it will allow exploration of the covariance structure across tasks and domains. Covariation in these measures is predicted in all groups, reflecting developmental interdependence of low- and high-level cognitive processes. This covariation is predicted to be strongest in ASC group, reflecting a systems-level alteration in neural information processing that leads via altered interactive specialisation to differences in all task domains. In addition, the so-called “extreme male brain” conjecture on autism (Baron-Cohen 2002) would predict that sex differences in these measures within the normal group may recapitulate, to a lesser degree, the group differences between ASC and normal – indeed, there is a large literature on behavioural and physiological sex differences in the tasks in this paradigm (reviewed in Baron-Cohen et al. 2005), and very preliminary γ coherence measures in adults do suggest that long-range functional connectivity between brain regions may be greater in females than in males (Braeutigam et al. 2004). Interactions with age across the sample also will be studied, and may reveal a developmental effect on coherence akin to the known effects on ERP amplitudes and latencies.

3.3 Methods for Objective 3 (sharing data and methods, facilitating multi-site collaboration, communicating results): Source code and executable code for the game software, programmer-level and user-level documentation, and source code for all data analysis programs will be placed in a publicly accessible repository on the World Wide Web, and put in the public domain under the GNU General Public Licence. Diagnostic and psychometric data will be entered and maintained using the Internet System for Assessing Autistic Children (Hollander et al. 2004), or its successor database currently under development. In addition to these data, behavioural log files from the game, EEG data files, and structural MRI will be coded by subject number and either placed on the Web or, in the case of data files too large for the Web server, made available on DVD to all researchers who request them. MRI files will be anonymised by deletion of facial features. Work on the game will be publicised in the electronic newsletter of the International Society for Autism Research and at the Society's annual meeting, and contributions of program code, ideas for new game paradigms, and behavioural and/or physiological data will be solicited. Results and practical implications will be disseminated to central New York's autism community in a public meeting to be held annually at Cornell University, and by regular participation in other local forums such as those organised by the Racker Centers.

4. EXPECTED SIGNIFICANCE

Results from the proposed project are expected to have impact on the integrative study of perception, attention, and cognition in normal and disordered development, in the application of state-of-the-art methods in high-density EEG data acquisition and analysis, on the integration of research opportunities into the undergraduate curriculum, and on public understanding of the results and potential of research on developmental disorders and on cognitive neuroscience in general. The data acquired within the normal subject group, even by themselves, are expected to show how perceptual and cognitive capacities at high and low levels of processing covary in the context of normal development, and to further characterise ERP components in source terms of independent neural generators and their time courses, rather than purely observational terms of peak latencies and scalp distributions. The autism and sib group comparisons will provide crucial correlative data, illuminating the question of mutual dependence of deficits and superiorities across social and non-social domains – a question that has become particularly timely in light of behavioural genetic studies (Ronald et al. 2006ab) arguing for partial independence of genetic bases for these in the normal population.

A great potential significance of the proposed work rests in its comparison of behavioural and physiological variations within the normal group to those in the autistic and non-autistic sib groups, and what this comparison can say about the relation between normal cognitive variation and cognitive disorder: if the EEG data confirm the fMRI-based hypothesis of increased high-frequency activity within neural generators in autism families in general but decreased coherence between neural generators only in autism probands, this information on neural dynamics has the potential to further illuminate the question of what normal and abnormal development have in common, and how a familial liability can evolve into the full syndrome of a developmental disorder. (As a complement to this work, though outside the direct scope of this proposal, we are currently developing collaborative research in the neuropsychiatric genetics of autism, with a focus on integrating our behavioural and neurophysiological measures with assays of candidate genes whose various alleles may confer liability or protection.) Detailed physiological measurements on the the time courses of activity within and between individual neural generators can help explore the subtleties of this question, refining general notions of abnormal levels of brain activation to more specific characterisations in terms of early and late time courses and in terms of the moment-to-moment coherence of these activations across specific regions and generators.

A further area of significance is the expected impacts of this project on research within the undergraduate curriculum at Cornell, and on public awareness of cognitive neuroscience research in central New York. The project will provide opportunities for undergraduate training in behavioural assessment and neurophysiological studies of cognitive neuroscience, including the opportunity to for student research proposals to be carried through to implementation. In addition, the project will add an application to experimental science within Cornell's existing curriculum in video game design. Perhaps most importantly, the ongoing communication of results from this work to autism patients, parents, educators, and other members of the public will ground this work in relevance to real-world problems of autism services and education, and will showcase cognitive neuroscience's benefits to the public.

References

Allen G, Courchesne E. Attention function and dysfunction in autism. Frontiers in Bioscience 6:D105-119 (2001).

Barnea-Goraly N, Kwon H, Menon V, Eliez S, Lotspeich L, Reiss AL. White matter structure in autism: preliminary evidence from diffusion tensor imaging. Biological Psychiatry 55(3):323-326 (2004).

Baron-Cohen S. The extreme male brain theory of autism. Trends in Cognitive Sciences 6(6):248-254 (2002).

Baron-Cohen S. Mindblindness: an essay on autism and theory of mind. Cambridge, Massachusetts: MIT Press (1995).

Baron-Cohen S, Knickmeyer RC, Belmonte MK. Sex differences in the brain: implications for explaining autism. Science 310(5749):819-823 (2005).

Baron-Cohen S, Leslie AM, Frith U. Does the autistic child have a `theory of mind'? Cognition 21(1):37-46 (1985).

Baron-Cohen S, Hoekstra RA, Knickmeyer RC, Wheelwright S. The Autism-Spectrum Quotient (AQ) – adolescent version. Journal of Autism and Developmental Disorders 36(3):343-350 (2006).

Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I. The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. Journal of Child Psychology and Psychiatry 42(2):241-251 (2001).

Bell AJ, Sejnowski TJ. An information maximisation approach to blind separation and blind deconvolution. Neural Computation 7(6):1129-1159 (1995).

Belmonte MK. Shifts of visual spatial attention modulate a steady-state visual evoked potential. Cognitive Brain Research 6(4):295-307 (1998).

Belmonte MK. Abnormal attention in autism shown by steady-state visual evoked potentials. Autism 4(3):269-285 (2000).

Belmonte MK. Abnormal Visual Motion Processing as a Neural Endophenotype of Autism. Cahiers de Psychologie Cognitive / Current Psychology of Cognition 23(1-2):65-74 (2005).

Belmonte MK, Allen G, Beckel-Mitchener A, Boulanger LM, Carper RA, Webb SJ. Autism and abnormal development of brain connectivity. Journal of Neuroscience 24(42):9228-9231 (2004a).

Belmonte MK, Gomot M, Baron-Cohen S. Visual attention in autism families: 'unaffected' sibs share atypical frontal activation. Journal of Child Psychology and Psychiatry, in press (2008).

Belmonte MK, Bourgeron T. Fragile X syndrome and autism at the intersection of genetic and neural networks. Nature Neuroscience 9(10):1221-1225 (2006).

Belmonte MK, Cook EH Jr, Anderson GM, Rubenstein JL, Greenough WT, Beckel-Mitchener A, Courchesne E, Boulanger LM, Powell SB, Levitt PR, Perry EK, Jiang YH, DeLorey TM, Tierney E. Autism as a disorder of neural information processing: directions for research and targets for therapy. Molecular Psychiatry 9(7):646-663 (2004b). http://www.cureautismnow.org/conferences/summitmeetings/

Belmonte MK, Gomot M, Baron-Cohen S. Visual attention in autism families: 'unaffected' sibs share atypical frontal activation. Journal of Child Psychology and Psychiatry, in press (2008a).

Belmonte MK, Mazziotta JC, Minshew NJ, Evans AC, Courchesne E, Dager SR, Bookheimer SY, Aylward EH, Amaral DG, Cantor RM, Chugani DC, Dale AM, Davatzikos C, Fischbach GD, Gerig G, Herbert MR, Lainhart JE, Murphy DG, Piven J, Reiss AL, Schultz RT, Zeffiro TA, Levi-Pearl S, Lajonchere C, Colamarino SA. Offering to share: how to put heads together in autism neuroimaging. Journal of Autism and Developmental Disorders 38(1):2-13 (2008b).

Belmonte MK, Yurgelun-Todd DA. Permutation testing made practical for functional magnetic resonance image analysis. IEEE Transactions on Medical Imaging 20(3):243-248 (2001).

Belmonte MK, Yurgelun-Todd DA. Functional anatomy of impaired selective attention and compensatory processing in autism. Cognitive Brain Research 17(3):651-664 (2003).

Berka C, Levendowski DJ, Cvetinovic MM, Petrovic MM, Davis G, Lumicao MN, Zivkovic VT. Real-time analyses of EEG indexes of alertness, cognition and memory acquired with a wireless EEG headset. International Journal of Human-Computer Interaction 17(2):151-170 (2004).

Bertone E, Mottron L, Jelenic P, Faubert J. Motion perception in autism: a "complex" issue. Journal of Cognitive Neuroscience 15(2):226-235 (2003).

Bishop DV, Hardiman M, Uwer R, von Suchodoletz W. Maturation of the long-latency auditory ERP: step function changes at start and end of adolescence. Developmental Science 10(5):565-575 (2007).

Bodfish JW, Symons FJ, Parker DE, Lewis MH. Varieties of repetitive behavior in autism: comparisons to mental retardation. Journal of Autism and Developmental Disorders 30(3):237-243 (2000).

Braeutigam S, Rose SP, Swithenby SJ, Ambler T. The distributed neuronal systems supporting choice-making in real-life situations: differences between men and women when choosing groceries detected using magnetoencephalography. European Journal of Neuroscience 20(1):293-302 (2004).

Brock J, Brown CC, Boucher J, Rippon G. The temporal binding deficit hypothesis of autism. Development and Psychopathology 14(2):209-224 (2002).

Brookings JB, Wilson GF, Swain CR. Psychophysiological responses to changes in workload during simulated air traffic control. Biological Psychology 42(3):361-377 (1996).

Brown C, Gruber T, Boucher J, Rippon G, Brock J. Gamma abnormalities during perception of illusory figures in autism. Cortex 41(3):364-376 (2005).

Buchwald JS, Erwin R, Van Lancker D, Guthrie D, Schwafel J, Tanguay P. Midlatency auditory evoked responses: P1 abnormalities in adult autistic subjects. Electroencephalography and Clinical Neurophysiology 84(2):164-171 (1992).

Burack JA. Selective attention deficits in persons with autism: preliminary evidence of an inefficient attentional lens. Journal of Abnormal Psychology 103(3):535-543 (1994).

Butler PD, Javitt DC. Early-stage visual processing deficits in schizophrenia. Current Opinion in Psychiatry 18:151-157 (2005).

Butler PD, Martinez A, Foxe JJ, Kim D, Zemon V, Silipo G, Mahoney J, Shpaner M, Jalbrzikowski M, Javitt DC. Subcortical visual dysfunction in schizophrenia drives secondary cortical impairments. Brain 130(2):417-430 (2007).

Castel AD, Pratt J, Drummond E. The effects of action video game experience on the time course of inhibition of return and the efficiency of visual search. Acta Psychologica 119(2):217-230 (2005).

Charman T. The relationship between joint attention and pretend play in autism. Development and Psychopathology 9(1):1-16 (1997).

Ciesielski KT, Courchesne E, Elmasian R. Effects of focused selective attention tasks on event-related potentials in autistic and normal individuals. Electroencephalography and Clinical Neurophysiology 75(3):207-220 (1990).

Constantino JN, Davis SA, Todd RD, Schindler MK, Gross MM, Brophy SL, Metzger LM, Shoushtari CS, Splinter R, Reich W. Validation of a brief quantitative measure of autistic traits: comparison of the Social Responsiveness Scale with the Autism Diagnostic Interview – Revised. Journal of Autism and Developmental Disorders 33(4):427–433 (2003).

Courchesne E, Pierce K. Why the frontal cortex in autism might be talking only to itself: local over-connectivity but long-distance disconnection. Current Opinion in Neurobiology 15(2):225-230 (2005).

Courchesne E, Townsend J, Akshoomoff NA, Saitoh O, Yeung-Courchesne R, Lincoln AJ, James HE, Haas RH, Schreibman L, Lau L. Impairment in shifting attention in autistic and cerebellar patients. Behavioral Neuroscience 108(5):848-865 (1994).

Dalton KM, Nacewicz BM, Alexander AL, Davidson RJ. Gaze-fixation, brain activation, and amygdala volume in unaffected siblings of individuals with autism. Biological Psychiatry 61(4):512-520 (2007).

Dalton KM, Nacewicz BM, Johnstone T, Schaefer HS, Gernsbacher MA, Goldsmith HH, Alexander AL, Davidson RJ. Gaze fixation and the neural circuitry of face processing in autism. Nature Neuroscience 8(4):519-526 (2005).

Dawson G, Estes A, Munson J, Schellenberg G, Bernier R, Abbott R. Quantitative assessment of autism symptom-related traits in probands and parents: Broader Phenotype Autism Symptom Scale. Journal of Autism and Developmental Disorders 37(3):523-536 (2007).

Dawson G, Webb SJ, Schellenberg GD, Dager S, Friedman S, Aylward E, Richards T. Defining the broader phenotype of autism: genetic, brain, and behavioral perspectives. Development and Psychopathology 14(3):581-611 (2002).

Delorme A, Makeig S. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. Journal of Neuroscience Methods 134(1):9-21 (2004).

Doucet ME, Gosselin F, Lassonde M, Guillemot JP, Lepore F. Development of visual-evoked potentials to radially modulated concentric patterns. NeuroReport 16(16):1753-1756 (2005).

Feng J, Spence I, Pratt J. Playing an action video game reduces gender differences in spatial cognition. Psychological Science 18(10):850-855 (2007).

Ferree TC, Luu P, Russell GS, Tucker DM. Scalp electrode impedance, infection risk, and EEG data quality. Clinical Neurophysiology 112(3):536-544 (2001).
Fitch RH, Tallal P. Neural mechanisms of language-based learning impairments: insights from human populations and animal models. Behavioral and Cognitive Neuroscience Reviews 2: 155-178 (2003).
Frith CD. What do imaging studies tell us about the neural basis of autism? Novartis Foundation Symposia 251:149-166 (2003).
Frith U, Happé F. Autism: beyond 'theory of mind'. Cognition 50(1-3):115-132 (1994).
Frund I, Busch NA, Schadow J, Korner U, Herrmann CS. From perception to action: phase-locked gamma oscillations correlate with reaction times in a speeded response task. BMC Neuroscience 8(1):27 (2007).
Fusar-Poli P, Broome MR. Conceptual issues in psychiatric neuroimaging. Current Opinion in Psychiatry 19(6):608-612 (2006).
Golan O, Baron-Cohen S. Systemizing empathy: teaching adults with Asperger syndrome or high-functioning autism to recognize complex emotions using interactive media. Development and Psychopathology 18(2):591-617 (2006).
Graner Ray S. Gender inclusive game design: Expanding the market. Hingham, Massachusetts: Charles River Media (2004).
Green CS, Bavelier D. Action video game modifies visual selective attention. Nature 423(6939):534-537 (2003).
Green CS, Bavelier D. Enumeration versus multiple object tracking: the case of action video game players. Cognition 101(1):217-245 (2006a).
Green CS, Bavelier D. Effect of action video games on the spatial distribution of visuospatial attention. Journal of Experimental Psychology - Human Perception and Performance 32(6):1465-1478 (2006b).
Green CS, Bavelier D. Action-video-game experience alters the spatial resolution of vision. Psychological Science 18(1):88-94 (2007).
Grice SJ, Spratling MW, Karmiloff-Smith A, Halit H, Csibra G, de Haan M, Johnson MH. Disordered visual processing and oscillatory brain activity in autism and Williams syndrome. NeuroReport 12(12):2697-700 (2001).
Happé F, Frith U. The weak coherence account: detail-focused cognitive style in autism spectrum disorders. Journal of Autism and Developmental Disorders 36(1):5-25 (2006).
Herbert MR, Ziegler DA, Makris N, Filipek PA, Kemper TL, Normandin JJ, Sanders HA, Kennedy DN, Caviness VS Jr. Localization of white matter volume increase in autism and developmental language disorder. Annals of Neurology 55(4):530-540 (2004).
Hill EL. Executive dysfunction in autism. Trends in Cognitive Sciences 8(1):26-32 (2004).
Hollander E, Phillips A, King BH, Guthrie D, Aman MG, Law P, Owley T, Robinson R. Impact of recent findings on study design of future autism clinical trials. CNS Spectrums 9(1):49-56 (2004).
Hughes C, Russell J, Robbins TW. Evidence for executive dysfunction in autism. Neuropsychologia 32(4):477-492 (1994).
Jarrold C, Butler DW, Cottington EM, Jimenez F. Linking theory of mind and central coherence bias in autism and in the general population. Developmental Psychology 36(1):126-138 (2000).
Johnson MH, Halit H, Grice SJ, Karmiloff-Smith A. Neuroimaging of typical and atypical development: a perspective from multiple levels of analysis. Development and Psychopathology 14(3):521-536 (2002).
Johnson MH, Griffin R, Csibra G, Halit H, Farroni T, de Haan M, Tucker LA, Baron-Cohen S, Richards J. The emergence of the social brain network: evidence from typical and atypical development. Development and Psychopathology 17(3):599-619 (2005).
Just MA, Cherkassky VL, Keller TA, Minshew NJ. Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain 127(8):1811-1821 (2004).
Karmiloff-Smith A. Atypical epigenesis. Developmental Science 10(1):84-88 (2007).
Kemner C, Verbaten MN, Cuperus JM, Camfferman G, Van Engeland H. Visual and somatosensory event-related brain potentials in autistic children and three different control groups. Electroencephalography and Clinical Neurophysiology 92(3):225-237 (1994).
Lam KSL, Aman G. The Repetitive Behavior Scale – Revised: independent validation in persons with autism spectrum disorders. Journal of Autism and Developmental Disorders (in press 2007).
Leitman DI, Hoptman MJ, Foxe JJ, Saccente E, Wylie GR, Nierenberg J, Jalbrzikowski M, Lim KO, Javitt DC. The

neural substrates of impaired prosodic detection in schizophrenia and its sensorial antecedents. American Journal of Psychiatry 164(3):474-482 (2007).
Lieberman HR, Pentland AP. Microcomputer-based estimation of psychophysical thresholds: the best PEST. Behavior Research Methods and Instrumentation 14(1):21–25 (1982).
Lincoln AJ, Courchesne E, Harms L, Allen M. Contextual probability evaluation in autistic, receptive developmental language disorder, and control children: event-related brain potential evidence. Journal of Autism and Developmental Disorders 23(1):37-58 (1993).
Lincoln AJ, Courchesne E, Harms L, Allen M. Sensory modulation of auditory stimuli in children with autism and receptive developmental language disorder: event-related brain potential evidence. Journal of Autism and Developmental Disorders 25(5):521-39 (1995).
Lord C, Risi S, Lambrecht L, Cook EH Jr, Leventhal BL, DiLavore PC, Pickles A, Rutter M. The Autism Diagnostic Observation Schedule - Generic: a standard measure of social and communication deficits associated with the spectrum of autism. Journal of Autism and Developmental Disorders 30(3):205-223 (2000).
Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview - Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. Journal of Autism and Developmental Disorders 24(5):659-685 (1994).
Makeig S, Delorme A, Westerfield M, Jung TP, Townsend J, Courchesne E, Sejnowski TJ. Electroencephalographic brain dynamics following manually responded visual targets. PLoS Biology 2(6):e176 (2004).
Makeig S, Westerfield M, Jung TP, Enghoff S, Townsend J, Courchesne E, Sejnowski TJ. Dynamic brain sources of visual evoked responses. Science 295(5555):690-694 (2002).
Milne E, Swettenham J, Hansen P, Campbell R, Jeffries H, Plaisted K. High motion coherence thresholds in children with autism. Journal of Child Psychology and Psychiatry 43(2):255-263 (2002).
Minshew NJ, Hobson JA. Sensory sensitivities and performance on sensory perceptual tasks in high-functioning individuals with autism. Journal of Autism and Developmental Disorders, in press (2008).
Molholm S, Ritter W, Murray MM, Javitt DC, Schroeder CE, Foxe JJ. Multisensory auditory-visual interactions during early sensory processing in humans: a high-density electrical mapping study. Cognitive Brain Research 14(1):115-128 (2002).
Mottron L, Dawson M, Soulières I, Hubert B, Burack JA. Enhanced perceptual functioning in autism: an update, and eight principles of autistic perception. Journal of Autism and Developmental Disorders 36(1):27-43 (2006).
Mueller V, Brehmer Y, von Oertzen T, Li S, Lindenberger U. Electrophysiological correlates of selective attention: a lifespan comparison. BMC Neuroscience 9:18 (2008).
Müller MM, Junghofer M, Elbert T, Rochstroh B. Visually induced gamma-band responses to coherent and incoherent motion: a replication study. NeuroReport 8(11):2575-2579 (1997).
Ozonoff S, Strayer DL, McMahon WM, Filloux F. Executive function abilities in autism and Tourette syndrome: an information processing approach. Journal of Child Psychology and Psychiatry 35(6):1015-1032 (1994).
Pellicano E, Gibson L, Maybery M, Durkin K, Badcock DR. Abnormal global processing along the dorsal visual pathway in autism: a possible mechanism for weak visuospatial coherence? Neuropsychologia 43(7):1044-1053 (2005).
Pentland AP. Maximum likelihood estimation: the best PEST. Perception and Psychophysics 28(4):377-379 (1980).
Peterson CC, Siegal M. Representing inner worlds: Theory of Mind in autistic, deaf and normal hearing children. Psychological Science 10(2):126-129 (1999).
Piven J, Palmer P, Jacobi D, Childress D, Arndt S. Broader autism phenotype: evidence from a family history study of multiple-incidence autism families. American Journal of Psychiatry 154(2):185-190 (1997).
Plaisted K, O'Riordan M, Baron-Cohen S. Enhanced visual search for a conjunctive target in autism: a research note. Journal of Child Psychology and Psychiatry 39(5):777-783 (1998).
Plaisted K, Saksida L, Alcantara J, Weisblatt E. Towards an understanding of the mechanisms of weak central coherence effects: experiments in visual configural learning and auditory perception. Philosophical Transactions of the Royal Society of London B 358(1430):375-386 (2003).
Plaisted K, Swettenham J, Rees L. Children with autism show local precedence in a divided attention task and global precedence in a selective attention task. Journal of Child Psychology and Psychiatry 40(5):733-742 (1999).
Pompe MT, Kranjc BS, Brecelj J. Visual evoked potentials to red-green stimulation in schoolchildren. Visual Neuroscience 23(3-4):447-451 (2006).

Ponton CW, Eggermont JJ, Kwong B, Don M. Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. Clinical Neurophysiology 111(2):220-236 (2000).

Posner MI, Walker JA, Friedrich FA, Rafal RD. How do the parietal lobes direct covert attention? Neuropsychologia 25(1A):135-145 (1987).

Rinehart NJ, Tonge BJ, Bradshaw JL, Iansek R, Enticott PG, Johnson KA. Movement-related potentials in high-functioning autism and Asperger's disorder. Developmental Medicine and Child Neurology 48(4):272-277 (2006).

Rogers SJ, Ozonoff S. What do we know about sensory dysfunction in autism? A critical review of the empirical evidence. Journal of Child Psychology and Psychiatry 46(12):1255-1268 (2005).

Ronald A, Happé F, Bolton P, Butcher LM, Price TS, Wheelwright S, Baron-Cohen S, Plomin R. Genetic heterogeneity between the three components of the autism spectrum: a twin study. Journal of the American Academy of Child and Adolescent Psychiatry 45(6):691-699 (2006a).

Ronald A, Happé F, Price TS, Baron-Cohen S, Plomin R. Phenotypic and genetic overlap between autistic traits at the extremes of the general population. Journal of the American Academy of Child and Adolescent Psychiatry 45(10):1206-1214 (2006b).

Schmidt GR, Belmonte MK. Scalable, content-based audio identification by multiple independent psychoacoustic matching. Journal of the Audio Engineering Society 52(4):366-377 (2004).

Senkowski D, Talsma D, Grigutsch M, Herrmann CS, Woldorff MG. Good times for multisensory integration: effects of the precision of temporal synchrony as revealed by gamma-band oscillations. Neuropsychologia 45(3):561-571 (2007).

Shah A, Frith U. Why do autistic individuals show superior performance on the block design task? Journal of Child Psychology and Psychiatry 34(8):1351-1364 (1993).

Smith ME, McEvoy LK, Gevins A. Neurophysiological indices of strategy development and skill acquisition. Cognitive Brain Research 7(3):389-404 (1999).

Spencer J, O'Brien J, Riggs K, Braddick O, Atkinson J, Wattam-Bell J. Motion processing in autism: evidence for a dorsal-stream deficiency. NeuroReport 11(12):2765-2767 (2000).

St John M, Kobus DA, Morrison JG. A multi-tasking environment for manipulating and measuring neural correlates of cognitive workload. In: Proceedings of the 2002 IEEE 7th Conference on Human Factors and Power Plants. pp 7.10-7.14. New York: IEEE (2002).

St John M, Kobus DA, Morrison JG, Schmorrow D. Overview of the DARPA augmented cognition technical integration experiment. International Journal of Human-Computer Interaction 17(2):131-149 (2004).

Tallal P, Miller SL, Bedi G, Byma G, Wang X, Nagarajan SS, Schreiner C, Jenkins WM, Merzenich MM. Language comprehension in language-learning impaired children improved with acoustically modified speech. Science 271(5245):81-84 (1996).

Tallal P. Improving language and literacy is a matter of time. Nature Reviews Neuroscience 5(9):721-728 (2004).

Tallon-Baudry C, Bertrand O. Oscillatory gamma activity in humans and its role in object representation. Trends in Cognitive Sciences 3(4):151-162 (1999).

Townsend J, Adamo M, Haist F. Changing channels: an fMRI study of aging and cross-modal attention shifts. NeuroImage 31(4):1682-1692 (2006).

Townsend J, Courchesne E. Parietal damage and narrow "spotlight" spatial attention. Journal of Cognitive Neuroscience 6(3):220-232 (1994).

Townsend J, Harris NS, Courchesne E. Visual attention abnormalities in autism: delayed orienting to location. Journal of the International Neuropsychological Society 2(6):541-550 (1996).

Uhlhaas PJ, Silverstein SM. Perceptual organization in schizophrenia spectrum disorders: a review of empirical research and associated theories. Psychological Bulletin 131:618-632 (2005).

Uhlhaas PJ, Phillips WA, Schenkel LS, Silverstein SM. Theory of mind and perceptual context-processing in schizophrenia. Cognitive Neuropsychiatry 11(4):416-436 (2006).

von Ahn L. Games with a purpose. Computer 39(6):92-94 (2006).

Witkin HA. Individual differences in ease of perception of embedded figures. Journal of Personality 19(1):1-15 (1950).

BIOGRAPHICAL SKETCH – Matthew K Belmonte

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Cornell University, Ithaca, New York 14853-4401 mkb4@cornell.edu

Professional Preparation

Cornell University	English and computer science	BA	1990
University of California San Diego	neurosciences	MS	1994
Sarah Lawrence College	fiction	MFA	1998
Boston University	behavioural neuroscience	PhD	2001
University of Cambridge	brain imaging	postdoctoral	2002 - 2006

Appointments

2006 -	Assistant Professor, Department of Human Development, Cornell University
2002 - 2006	Senior Research Associate, Autism Research Centre, University of Cambridge
2001 - 2002	Senior Research Scientist, Tuneprint Corporation (Cambridge, Massachusetts)
1996 - 1998	Scientific Programmer, Howard Hughes Medical Institute, New York University

Publications Closely Related to the Proposed Project:

Belmonte MK, Gomot M, Baron-Cohen S. Visual attention in autism families: 'unaffected' sibs share atypical frontal activation. *Journal of Child Psychology and Psychiatry,* in press.

Belmonte MK, Carper RA. Monozygotic twins with Asperger syndrome: differences in behaviour reflect variations in brain structure and function. *Brain and Cognition* **61**(1):110-121 (2006).

Belmonte MK, Allen G, Beckel-Mitchener A, Boulanger LM, Carper RA, Webb SJ. Autism and abnormal development of brain connectivity. *Journal of Neuroscience* **24**(42):9228-9231 (2004).

Belmonte MK, Yurgelun-Todd DA. Functional anatomy of impaired selective attention and compensatory processing in autism. *Cognitive Brain Research* **17**(3):651-664 (2003).

Belmonte MK. Abnormal attention in autism shown by steady-state visual evoked potentials. Autism **4**(3):269-285 (2000).

Other Publications:

Belmonte MK, Mazziotta JC, Minshew NJ, Evans AC, Courchesne E, Dager SR, Bookheimer SY, Aylward EH, Amaral DG, Cantor RM, Chugani DC, Dale AM, Davatzikos C, Gerig G, Herbert MR, Lainhart JE, Murphy DG, Piven J, Reiss AL, Schultz RT, Zeffiro TA, Levi-Pearl S, Lajonchere C, Colamarino SA. Offering to share: how to put heads together in autism neuroimaging. *Journal of Autism and Developmental Disorders* **38**(1):2-13 (2008).

Belmonte MK, Bourgeron T. Fragile X syndrome and autism at the intersection of genetic and neural networks. *Nature Neuroscience* **9**(10):1221-1225 (2006).

Belmonte MK, Cook EH Jr, Anderson GM, Rubenstein JLR, Greenough WT, Beckel-Mitchener A, Courchesne E, Boulanger LM, Powell SB, Levitt PR, Perry EK, Jiang Y, DeLorey TM, Tierney E. Autism as a disorder of neural information processing: directions for research and targets for therapy. *Molecular Psychiatry* **9**(7):646-663 (2004).

Belmonte MK, Yurgelun-Todd DA. Anatomic dissociation of selective and suppressive processes in visual attention. *NeuroImage* **19**(1):180-189 (2003).

Belmonte MK, Yurgelun-Todd DA. Permutation testing made practical for functional magnetic resonance image analysis. *IEEE Transactions on Medical Imaging* **20**(3):243-248 (2001).

All publications are available electronically from http://www.mit.edu/~belmonte/

Synergistic Activities: 1. Teaching: Instructor and developer of neuroscience and computer science curricula for high school students (Johns Hopkins University Center for Talented Youth, 1987-1997; MIT Educational Studies Program, 1999-2000; Duke University Talent Identification Program, 1998-2001). Writing-in-the-disciplines instructor at MIT (1999-2001), incorporating writing instruction in undergraduate science and engineering curricula. Supervisor in medical neurobiology at Cambridge (2002-2003). Mentor to ten undergraduate researchers (eight biologists, two computer scientists) at Cornell (2006-2008). Developed a writing-intensive undergraduate seminar "Autism and the Development of Social Cognition" at Cornell (fall 2006), taught from critical readings of primary research literature.

2. Outreach: Presenter at the Cornell Cooperative Extension Research Update, an annual meeting for New York

State educators on practical implications of research in human development. Frequent presenter on the relation between cognitive neuroscience and the arts (“Autism and Representation,” Case Western Reserve University, October 2005; “Literature and the Cognitive Sciences,” University of Connecticut, April 2006; “From the Brain to Human Culture,” Bucknell University, April 2007). Member, Scientific Advisory Committee, Helping Autism through Learning and Outreach (www.halo-soma.org, 2008-).

3. Research tools: Contributor to several public-domain software tools for neuroscience research and for general scientific computation, including AFNI (afni.nimh.nih.gov) and Netlib (www.netlib.org).

4. Scientific review: Member, Scientific Review Council, Cure Autism Now foundation (2002-2006). (Constituted of family members of people with autism, the Council sets policy, formulates research initiatives, and prioritises funding decisions.) Referee to UK Economic and Social Research Council (2004), UK Medical Research Council (2007, 2008), US National Institutes of Health (Autism Centers of Excellence, 2006), Netherlands Organisation for Scientific Research (2007), Autism Speaks (Innovative Technology for Autism, 2007).

5. Journals and meetings: Interim chair of Publications Committee, International Society for Autism Research (2006), and founding editorial board member (2007-), *Autism Research.* Referee to *American Journal of Psychiatry, Behavioral and Brain Sciences, Biological Psychiatry, Biological Reviews, Brain, Brain and Cognition,* Cambridge University Press, *Cell, Cerebral Cortex, Developmental Neuropsychology, European Archives of Psychiatry and Clinical Neuroscience, European Journal of Neuroscience, IEEE Transactions on Medical Imaging, Journal of the American Academy of Child and Adolescent Psychiatry, Journal of Autism and Developmental Disorders, Journal of Child Psychology and Psychiatry, Journal of Experimental Psychology: Human Perception and Performance, Journal of Neuroscience, Nature, Nature Neuroscience, NeuroImage, Neuron, Neuropsychologia, Neuroscience and Biobehavioral Reviews, PLoS Biology, Personality and Individual Differences, Proceedings of the National Academy of Sciences, Psychiatry Research: Neuroimaging, Review of General Psychology, Science, Trends in Cognitive Sciences, Trends in Neurosciences,* Yale University Press. Organiser of Cure Autism Now foundation consensus workshops on targeted research (2002) and on neuroimaging data sharing (2006). Organiser of 2004 Society for Neuroscience mini-symposium on “Autism and Abnormal Development of Brain Connectivity.”

<u>Collaborators and Co-Authors</u> (July 2006 - July 2008): Yael Adini, Weizmann Institute of Science. Natacha A Akshoomoff, University of California San Diego. David G Amaral, University of California Davis (MIND Institute). Christopher Ashwin, University of Essex. Elizabeth H Aylward, University of Washington. Simon Baron-Cohen, University of Cambridge. Frédéric A Bernard, University of Cambridge. Yoram S Bonneh, Weizmann Institute of Science. Susan Y Bookheimer, University of California Los Angeles. Thomas Bourgeron, Institut Pasteur. Edward T Bullmore, University of Cambridge. Jonathan Butler, MIT (Broad Institute) & Google, Inc. Rita M Cantor, University of California Los Angeles. Bhismadev Chakrabarti, University of Cambridge. Diane C Chugani, Children's Hospital of Michigan. Sophia A Colamarino, Autism Speaks. Eric Courchesne, University of California San Diego. Stephen R Dager, University of Washington. Anders M Dale, University of California San Diego. Christos Davatzikos, University of Pennsylvania. Alan C Evans, Montreal Neurological Institute. Karen Fried, Franziska Racker Centers (Ithaca, NY). Guido Gerig, University of Utah & University of North Carolina, Chapel Hill. Ofer Golan, Bar-Ilan University. Marie Gomot, Université François-Rabelais. Martha R Herbert, Massachusetts General Hospital. John F Houde, University of California San Francisco. Portia E Iversen, Autism Speaks. David B Jaffe, MIT (Broad Institute). Tal Kenet, Massachusetts General Hospital. Michael Kleber, MIT (Broad Institute) & Google, Inc. Janet E Lainhart, University of Utah. Clara Lajonchere, Autism Speaks. Eric S Lander, MIT (Broad Institute). Susan Levi-Pearl, Tourette Syndrome Association. Iain MacCallum, MIT (Broad Institute). John C Mazziotta, University of California Los Angeles. Michael M Merzenich, University of California San Francisco. Nancy J Minshew, University of Pittsburgh. Christopher I Moore, MIT. Declan G Murphy, King's College London (Institute of Psychiatry). Chad Nusbaum, MIT (Broad Institute). Francesca Pei, Istituto “Stella Maris” (Pisa). Rosalind Picard, MIT Media Laboratory. Joseph Piven, University of North Carolina, Chapel Hill. Allan L Reiss, Stanford University. Ilya A Shlyakhter, MIT (Broad Institute). Robert T Schultz, Yale University. David I Schwartz, Rochester Institute of Technology. Helen J Simon, Smith-Kettlewell Eye Research Institute. Tristram Smith, University of Rochester Strong Memorial Hospital. Jeanne Townsend, University of California Dan Diego. Walker M White, Cornell University. Thomas A Zeffiro, Massachusetts General Hospital.

<u>Graduate Advisors and Postdoctoral Sponsors:</u> Simon Baron-Cohen (University of Cambridge), Eric Courchesne (University of California San Diego), Joan Silber (Sarah Lawrence College), Deborah Yurgelun-Todd (McLean Hospital, now at the University of Utah).

<u>Thesis Advisor and Postgraduate-Scholar Sponsor</u>: none.

SUMMARY PROPOSAL BUDGET

YEAR 1

ORGANIZATION: **Cornell University - State**				FOR NSF USE ONLY — PROPOSAL NO.	DURATION (months): Proposed / Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Matthew K Belmonte**				AWARD NO.	

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Matthew K Belmonte - Assistant Professor**	0.00	0.00	1.00	$ **10,179**	$
2.					
3.					
4.					
5.					
6. (**0**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	**0**	
7. (**1**) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	1.00	**10,179**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**1**) POST DOCTORAL SCHOLARS	12.00	0.00	0.00	**36,996**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	**0**	
3. (**0**) GRADUATE STUDENTS				**0**	
4. (**0**) UNDERGRADUATE STUDENTS				**0**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**0**) OTHER				**0**	
TOTAL SALARIES AND WAGES (A + B)				**47,175**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**21,276**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**68,451**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				**0**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**5,000**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
TOTAL NUMBER OF PARTICIPANTS (**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**0**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**0**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**0**	
5. SUBAWARDS				**0**	
6. OTHER				**32,608**	
TOTAL OTHER DIRECT COSTS				**32,608**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**106,059**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **Modified Total Direct Costs - year 1 (Rate: 54.0000, Base: 106059)**					
TOTAL INDIRECT COSTS (F&A)				**57,272**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**163,331**	
K. RESIDUAL FUNDS				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **163,331**	$
M. COST SHARING PROPOSED LEVEL $ **0**	AGREED LEVEL IF DIFFERENT $				

PI/PD NAME: **Matthew K Belmonte**	FOR NSF USE ONLY — INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

SUMMARY PROPOSAL BUDGET

YEAR 2

FOR NSF USE ONLY					
PROPOSAL NO.	DURATION (months)				
	Proposed	Granted			
AWARD NO.					

ORGANIZATION
Cornell University - State

PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR
Matthew K Belmonte

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Matthew K Belmonte - Assistant Professor**	0.00	0.00	1.00	$ **10,688**	$
2.					
3.					
4.					
5.					
6. (**0**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	**0**	
7. (**1**) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	1.00	**10,688**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**1**) POST DOCTORAL SCHOLARS	12.00	0.00	0.00	**38,846**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	**0**	
3. (**1**) GRADUATE STUDENTS				**30,634**	
4. (**0**) UNDERGRADUATE STUDENTS				**0**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**0**) OTHER				**0**	
TOTAL SALARIES AND WAGES (A + B)				**80,168**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**22,340**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**102,508**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				**0**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**1,854**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS					
1. STIPENDS $ **0**					
2. TRAVEL **0**					
3. SUBSISTENCE **0**					
4. OTHER **0**					
TOTAL NUMBER OF PARTICIPANTS (**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**0**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**0**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**0**	
5. SUBAWARDS				**0**	
6. OTHER				**40,706**	
TOTAL OTHER DIRECT COSTS				**40,706**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**145,068**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **Modified Total Direct costs - year 2 (Rate: 54.0000, Base: 131284)**					
TOTAL INDIRECT COSTS (F&A)				**70,893**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**215,961**	
K. RESIDUAL FUNDS				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **215,961**	$

M. COST SHARING PROPOSED LEVEL $ **0** AGREED LEVEL IF DIFFERENT $

PI/PD NAME	FOR NSF USE ONLY		
Matthew K Belmonte	INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

SUMMARY PROPOSAL BUDGET

YEAR 3

ORGANIZATION **Cornell University - State**				FOR NSF USE ONLY PROPOSAL NO.	DURATION (months) Proposed / Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR **Matthew K Belmonte**				AWARD NO.	

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Matthew K Belmonte - none**	0.00	0.00	1.00	$ **11,222**	$
2.					
3.					
4.					
5.					
6. (**0**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	**0**	
7. (**1**) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	1.00	**11,222**	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (**1**) POST DOCTORAL SCHOLARS	12.00	0.00	0.00	**40,788**	
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	**0**	
3. (**1**) GRADUATE STUDENTS				**32,166**	
4. (**0**) UNDERGRADUATE STUDENTS				**0**	
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**	
6. (**0**) OTHER				**0**	
TOTAL SALARIES AND WAGES (A + B)				**84,176**	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**23,457**	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**107,633**	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				**0**	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**1,910**	
2. FOREIGN				**0**	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ **0** 2. TRAVEL **0** 3. SUBSISTENCE **0** 4. OTHER **0**					
TOTAL NUMBER OF PARTICIPANTS (**0**) TOTAL PARTICIPANT COSTS				**0**	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				**0**	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**3,000**	
3. CONSULTANT SERVICES				**0**	
4. COMPUTER SERVICES				**0**	
5. SUBAWARDS				**0**	
6. OTHER				**42,130**	
TOTAL OTHER DIRECT COSTS				**45,130**	
H. TOTAL DIRECT COSTS (A THROUGH G)				**154,673**	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **Modified Total Direct costs - year 3 (Rate: 54.0000, Base: 140200)**					
TOTAL INDIRECT COSTS (F&A)				**75,708**	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**230,381**	
K. RESIDUAL FUNDS				**0**	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **230,381**	$
M. COST SHARING PROPOSED LEVEL $ **0**	AGREED LEVEL IF DIFFERENT $				

PI/PD NAME **Matthew K Belmonte**	FOR NSF USE ONLY INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

SUMMARY PROPOSAL BUDGET

YEAR 4

ORGANIZATION **Cornell University - State**				FOR NSF USE ONLY PROPOSAL NO.	DURATION (months) Proposed / Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR **Matthew K Belmonte**				AWARD NO.	

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. **Matthew K Belmonte - Assistant Professor**	0.00	0.00	1.00	$ 11,783	$
2.					
3.					
4.					
5.					
6. (0) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (1) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	1.00	11,783	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (0) POST DOCTORAL SCHOLARS	0.00	0.00	0.00	0	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (1) GRADUATE STUDENTS				33,774	
4. (0) UNDERGRADUATE STUDENTS				0	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (0) OTHER				0	
TOTAL SALARIES AND WAGES (A + B)				45,557	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				5,314	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				50,871	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				1,967	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 0 2. TRAVEL 0 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (0) TOTAL PARTICIPANT COSTS				0	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				0	
3. CONSULTANT SERVICES				0	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				43,612	
TOTAL OTHER DIRECT COSTS				43,612	
H. TOTAL DIRECT COSTS (A THROUGH G)				96,450	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **Modified Total Direct costs - year 4 (Rate: 54.0000, Base: 81254)**					
TOTAL INDIRECT COSTS (F&A)				43,877	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				140,327	
K. RESIDUAL FUNDS				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 140,327	$
M. COST SHARING PROPOSED LEVEL $ 0	AGREED LEVEL IF DIFFERENT $				

PI/PD NAME **Matthew K Belmonte**	FOR NSF USE ONLY INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

 ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

SUMMARY PROPOSAL BUDGET

YEAR 5

ORGANIZATION: **Cornell University - State**				FOR NSF USE ONLY		
				PROPOSAL NO.	DURATION (months) Proposed	Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR: **Matthew K Belmonte**				AWARD NO.		
A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)	
1. **Matthew K Belmonte - Assistant Professor**	0.00	0.00	1.00	$ **12,373**	$	
2.						
3.						
4.						
5.						
6. (**0**) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	**0**		
7. (**1**) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	1.00	**12,373**		
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)						
1. (**0**) POST DOCTORAL SCHOLARS	0.00	0.00	0.00	**0**		
2. (**0**) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	**0**		
3. (**1**) GRADUATE STUDENTS				**35,462**		
4. (**0**) UNDERGRADUATE STUDENTS				**0**		
5. (**0**) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				**0**		
6. (**0**) OTHER				**0**		
TOTAL SALARIES AND WAGES (A + B)				**47,835**		
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				**5,580**		
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				**53,415**		
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)						
TOTAL EQUIPMENT				**0**		
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				**2,026**		
2. FOREIGN				**0**		
F. PARTICIPANT SUPPORT COSTS						
1. STIPENDS $ **0**						
2. TRAVEL **0**						
3. SUBSISTENCE **0**						
4. OTHER **0**						
TOTAL NUMBER OF PARTICIPANTS (**0**) TOTAL PARTICIPANT COSTS				**0**		
G. OTHER DIRECT COSTS						
1. MATERIALS AND SUPPLIES				**0**		
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				**3,000**		
3. CONSULTANT SERVICES				**0**		
4. COMPUTER SERVICES				**0**		
5. SUBAWARDS				**0**		
6. OTHER				**15,956**		
TOTAL OTHER DIRECT COSTS				**18,956**		
H. TOTAL DIRECT COSTS (A THROUGH G)				**74,397**		
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE) **Modified Total Direct costs - year 5 (Rate: 54.0000, Base: 58441)**						
TOTAL INDIRECT COSTS (F&A)				**31,558**		
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				**105,955**		
K. RESIDUAL FUNDS				**0**		
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ **105,955**	$	
M. COST SHARING PROPOSED LEVEL $ **0**	AGREED LEVEL IF DIFFERENT $					
PI/PD NAME: **Matthew K Belmonte**				FOR NSF USE ONLY		
				INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*				Date Checked	Date Of Rate Sheet	Initials - ORG

 *ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET

SUMMARY PROPOSAL BUDGET

Cumulative

ORGANIZATION Cornell University - State				FOR NSF USE ONLY PROPOSAL NO.	DURATION (months) Proposed / Granted
PRINCIPAL INVESTIGATOR / PROJECT DIRECTOR Matthew K Belmonte				AWARD NO.	

A. SENIOR PERSONNEL: PI/PD, Co-PI's, Faculty and Other Senior Associates (List each separately with title, A.7. show number in brackets)	NSF Funded Person-months CAL	ACAD	SUMR	Funds Requested By proposer	Funds granted by NSF (if different)
1. Matthew K Belmonte - none	0.00	0.00	5.00	$ 56,245	$
2.					
3.					
4.					
5.					
6. ( ) OTHERS (LIST INDIVIDUALLY ON BUDGET JUSTIFICATION PAGE)	0.00	0.00	0.00	0	
7. (1) TOTAL SENIOR PERSONNEL (1 - 6)	0.00	0.00	5.00	56,245	
B. OTHER PERSONNEL (SHOW NUMBERS IN BRACKETS)					
1. (3) POST DOCTORAL SCHOLARS	36.00	0.00	0.00	116,630	
2. (0) OTHER PROFESSIONALS (TECHNICIAN, PROGRAMMER, ETC.)	0.00	0.00	0.00	0	
3. (4) GRADUATE STUDENTS				132,036	
4. (0) UNDERGRADUATE STUDENTS				0	
5. (0) SECRETARIAL - CLERICAL (IF CHARGED DIRECTLY)				0	
6. (0) OTHER				0	
TOTAL SALARIES AND WAGES (A + B)				304,911	
C. FRINGE BENEFITS (IF CHARGED AS DIRECT COSTS)				77,967	
TOTAL SALARIES, WAGES AND FRINGE BENEFITS (A + B + C)				382,878	
D. EQUIPMENT (LIST ITEM AND DOLLAR AMOUNT FOR EACH ITEM EXCEEDING $5,000.)					
TOTAL EQUIPMENT				0	
E. TRAVEL 1. DOMESTIC (INCL. CANADA, MEXICO AND U.S. POSSESSIONS)				12,757	
2. FOREIGN				0	
F. PARTICIPANT SUPPORT COSTS 1. STIPENDS $ 0 2. TRAVEL 0 3. SUBSISTENCE 0 4. OTHER 0					
TOTAL NUMBER OF PARTICIPANTS (0) TOTAL PARTICIPANT COSTS				0	
G. OTHER DIRECT COSTS					
1. MATERIALS AND SUPPLIES				0	
2. PUBLICATION COSTS/DOCUMENTATION/DISSEMINATION				6,000	
3. CONSULTANT SERVICES				0	
4. COMPUTER SERVICES				0	
5. SUBAWARDS				0	
6. OTHER				175,012	
TOTAL OTHER DIRECT COSTS				181,012	
H. TOTAL DIRECT COSTS (A THROUGH G)				576,647	
I. INDIRECT COSTS (F&A)(SPECIFY RATE AND BASE)					
TOTAL INDIRECT COSTS (F&A)				279,308	
J. TOTAL DIRECT AND INDIRECT COSTS (H + I)				855,955	
K. RESIDUAL FUNDS				0	
L. AMOUNT OF THIS REQUEST (J) OR (J MINUS K)				$ 855,955	$
M. COST SHARING PROPOSED LEVEL $ 0 AGREED LEVEL IF DIFFERENT $					

PI/PD NAME Matthew K Belmonte	FOR NSF USE ONLY INDIRECT COST RATE VERIFICATION		
ORG. REP. NAME*	Date Checked	Date Of Rate Sheet	Initials - ORG

C ***ELECTRONIC SIGNATURES REQUIRED FOR REVISED BUDGET**

Budget justification – Belmonte, "CAREER: Integrative Behavioural and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments"

SENIOR PERSONNEL

1. Matthew Belmonte, 1 month summer salary
   Belmonte will supervise the project, including undergraduate, postgraduate and postdoctoral personnel. Funds are requested for one month of summer salary and fringe benefits (45.1%) in each year. Academic-year salary is covered by institutional funds.

OTHER PERSONNEL

1. One graduate student
   It is anticipated that the wide array of data collected in the course of this project will form the bases of at least one graduate student dissertation which can mine the data set for correlative relationships between task domains and between behavioural and electrophysiological traits. Funds are requested to support one graduate student for the duration of the project, except for an initial academic year during which departmental support is available. Current graduate stipend costs of $6,600 for the summer and $22,575 for the academic year have been extrapolated for these future years with 5% annual rises.
2. One postdoctoral scientist
   A three-year postdoctoral fellow with postgraduate experience in EEG recording and multivariate EEG data analysis will work with students in data collection and will implement data analytic software. The fellow will receive training in research diagnostic instruments for autism and opportunities for development in EEG data analytical methods and their application to normative and disordered populations. The postdoctoral fellow will assist not only with the development and implementation of data analytic tools and strategies, but also with technical aspects of EEG data recording. The standard $36,996 NRSA salary is budgeted, with 5% annual rises.

TRAVEL

1. Travel to ADI-R and ADOS-G diagnostic training, for 2 people
   The Autism Diagnostic Interview – Revised and the Autism Diagnostic Observation Schedule – Generic are the standard diagnostic instruments for autism. The postdoctoral scientist and the graduate student will travel to receive training on these instruments.
2. Meetings
   Funds are requested for yearly travel to the annual meeting of the Society for Neuroscience or a similar conference (e.g. the annual meeting of the Cognitive Neuroscience Society), at $1800 plus 3% p.a. inflation.

OTHER DIRECT COSTS

1. Publication costs
   We budget for two articles at the currently typical open-access publishing rate of $3000 per article.
2. ADI-R and ADOS-G diagnostic training, for 2 people
   Training for each of these two diagnostic instruments costs $1600 per person, for each of one graduate student and one postdoctoral fellow.
3. Graduate student tuition and insurance
   Funding is requested for tuition and insurance fees for the one graduate student listed under PERSONNEL above. Both of these expenses are part of the compensation package offered to all graduate students in the Department of Human Development. Tuition has been projected to be $11,550 for the academic year and health insurance has been budgeted at $1576 for the entire year. The first year's support is available from the department. Future years are extrapolated with annual rises of 5%.
4. Subject fees
   We request $100 per subject, for each of 24 subjects per year (approximately eight each in the autism, sib, and control groups) for each of the first four years, to compensate families for their time in behavioural and EEG recording at Cornell and MRI scanning at the Rochester

Center for Brain Imaging. As Rochester is 96 miles from Cornell by road, this commitment on the part of subjects and their parents is very significant and we want to be able to compensate them fairly.

5. Subject travel

We request funding for one return trip to Rochester, 192 miles at the Cornell fleet rate of 58½¢/mile, for a total of $113 per subject. We also request transport to Cornell for an average of three visits for each subject, at $33 (56 miles average) per return trip. Ithaca is a rural area, subjects are spread all over Tompkins and surrounding counties, and many of the distances involved will be large. This travel total of $212 is multiplied by 24 subjects per year for each of the first four years to yield $5088, with annual adjustments for inflation.

6. MRI scanning

The Rochester Center for Brain Imaging charges $780 per hour, and our protocol plus positioning time requires one hour of imaging time per subject. For 24 subjects per year these scanning fees total $18,720, with annual adjustments for inflation.

FACILITIES AND ADMINISTRATIVE COSTS (F&A)

F&A Costs have been proposed at a rate of 54% of the Modified Total Direct Cost (MTDC) as approved in Cornell's rate agreement with DHHS dated 6/19/08. A copy of this agreement can be found at http://www.accounting.cornell.edu/F&A_Cost_Rates.cfm. MTDC exclusions include Capital Equipment, GRA Allowance (tuition), health insurance, and subcontract costs in excess of $25,000 per subcontract.

Current and Pending Support

(See GPG Section II.C.2.h for guidance on information to include on this form.)

The following information should be provided for each investigator and other senior personnel. Failure to provide this information may delay consideration of this proposal.

Investigator: Matthew Belmonte

Other agencies (including NSF) to which this proposal has been/will be submitted.

Support: ☒ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: Video Game Environments for the Integrative Study of Perception, Attention and Social Cognition in Autism and Autism Sibs

Source of Support: Autism Speaks
Total Award Amount: $ 119,968 Total Award Period Covered: 08/01/08 - 07/31/10
Location of Project: Cornell University, Ithaca, NY
Person-Months Per Year Committed to the Project. Cal: 0.00 Acad: 0.45 Sumr: 0.00

Support: ☐ Current ☒ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title: CAREER: Integrative Behavioral and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments

Source of Support: National Science Foundation
Total Award Amount: $ 855,954 Total Award Period Covered: 06/01/09 - 05/31/14
Location of Project: Cornell University, Ithaca NY.
Person-Months Per Year Committed to the Project. Cal: 0.00 Acad: 0.45 Sumr: 1.00

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Sumr:

Support: ☐ Current ☐ Pending ☐ Submission Planned in Near Future ☐ *Transfer of Support

Project/Proposal Title:

Source of Support:
Total Award Amount: $ Total Award Period Covered:
Location of Project:
Person-Months Per Year Committed to the Project. Cal: Acad: Summ:

*If this project has previously been funded by another agency, please list and furnish information for immediately preceding funding period.

FACILITIES, EQUIPMENT & OTHER RESOURCES

FACILITIES: Identify the facilities to be used at each performance site listed and, as appropriate, indicate their capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Use "Other" to describe the facilities at any other performance sites listed and at sites for field studies. USE additional pages as necessary.

Laboratory: The Department of Human Development is installing a 128-channel BioSemi ActiveTwo EEG recording facility. This active electrode technology minimises noise from subject movement and other sources, and in our experience allows source analyses of very high quality. In addition to

Clinical: N/A

Animal: N/A

Computer: Computing support will be provided by the Department of Human Development.

Office: Office space and secretarial support will be provided by the Department of Human Development.

Other:

MAJOR EQUIPMENT: List the most important items available for this project and, as appropriate identifying the location and pertinent capabilities of each.

BioSemi ActiveTwo EEG system - 128 channels, active electrodes, located in the Department of Human Development, Martha Van Rensselaer Hall.

OTHER RESOURCES: Provide any information describing the other resources available for the project. Identify support services such as consultant, secretarial, machine shop, and electronics shop, and the extent to which they will be available for the project. Include an explanation of any consortium/contractual arrangements with other organizations.

Continuation Page:

LABORATORY FACILITIES (continued):

the recording room, the space includes desks for several students.

The Rochester Center for Brain Imaging, located 96 miles from Ithaca, houses a 3-Tesla Siemens Trio MRI scanner, and also a mock scanner for subject training. These facilities are accompanied by a support staff of magnetic resonance physicists, image analysts, and technicians, and are available to us on a fee-for-service basis. Rochester is a two-hour drive from Ithaca, making high-quality structural imaging possible in a day trip.

Cornell University
College of Human Ecology

Office of the Chairperson
Department of Human Development
G77 Martha Van Rensselaer Hall
Ithaca, New York 14853-4401
t. 607.255.7620
f. 607.255.9856

July 10, 2008

Faculty Early Career Development
CAREER Award
National Science Foundation

Dear Nomination Committee:

I am writing in strong and unequivocal support for the nomination of Dr. Matthew Belmonte for the National Science Foundation's CAREER Award. With this letter I verify that Dr. Belmonte is eligible for the CAREER program and I commit the Department of Human Development at Cornell University to fully support Dr. Belmonte's plan herein to integrate research and education in his scholarly work.

Dr. Belmonte is a recent faculty addition in Human Development. In reviewing the applicants for the departmental neuroscience position, the search committee unanimously and enthusiastically endorsed Dr. Belmonte as its first choice because of his demonstrated deep intellect and creative research ideas about developmental disorders, particularly autism spectrum disorders and Fragile X Syndrome. This was a highly competitive search with many excellent candidates; however, two of the most eminent international scholars in autism wrote letters of recommendation for Dr. Belmonte. His interview presentation was a tour de force, highly praised by faculty from throughout the university, including from the life and biologic sciences, neurobiology and behavior, education, psychology, and nutritional sciences. In a relatively brief time, Dr. Belmonte has established himself as one of the nation's foremost researchers of autism – an area that is presently exceedingly difficult to understand. Pondering his research findings in autism, which showed that the brains of autistic children and adults are characterized by delayed, weak communication across neural networks, a deficit that can affect a broad array of cognitive and emotional processes, Dr. Belmonte derived an integrative theory of autism that is a remarkable piece of cutting edge scholarship and, not surprisingly, was published in *Nature Neuroscience*, which has impact factor scores just below *Science* and *Nature*. Both his basic research findings and several integrative reviews appear in the very best scientific journals, including *Science, Journal of Neuroscience, Neuroimage, Molecular Psychiatry*, and *Annual Review of Neuroscience*.

In his application Dr. Belmonte outlines the integrative nature of his research in the neurosciences with education. From my vantage point I want to emphasize several points. Our undergraduate students, many of whom pursue graduate education in clinical psychology, education, law, and health/medicine, and our graduate students, many of whom seek professorial positions, will be greatly served by this CAREER Award to Dr. Belmonte. They take his large and popular neuroscience classes and seminars; they involve themselves as research assistants (39% of our undergraduates were engaged in research last year) or as honor students—and these numbers will only increase once his Game Design Initiative becomes available to them. The education efforts of Dr. Belmonte, however, will not end there. As the New York State land-grant institution, Cornell University has established an incredible and intricate network of extension and outreach efforts that extend far beyond the state to include national and international audiences—for example, podcasts, e-newsletters, brochures, outreach update conferences, and the University public relations team. Human Development has a tripartite mission: research, teaching, and outreach. Dr. Belmonte will have accessible to him this institutional commitment to form a wide, international network of dissemination and education. The impact of his scholarship will be immediate and profound.

Finally, as chair I established a mentoring committee to promote Dr. Belmonte's professional development. It is chaired by Dr. Richard Depue (neuroscientist) with Dr. Wendy Williams as an education expert and Dr. Steven Robertson as a teaching mentor. In their year-end report presented to the tenured departmental faculty, Dr. Belmonte's mentors wrote that he had "exceeded our expectations in the area of scholarship" and that he was well on the way to "further development as an internationally-recognized scholar."

We are extremely fortunate to have Dr. Belmonte at Cornell University because he is clearly a brilliant researcher and thinker. In is first year he established himself as a creative, demanding, and accessible scholar and we believe that he will inspire a generation of other young scholars to think like scientists and to have the passion and compassionate ability to convey this knowledge to others. In a few short years I am certain that the most eminent researchers in autism will look to Dr. Belmonte's research as cutting edge, innovative, and inspirational. There is no question that Dr. Belmonte will be a star in autism research in the near future.

Sincerely,

Ritch S-Wnz

Ritch C. Savin-Williams
Professor & Department Chair
Human Development
Cornell University

Cornell University
College of Human Ecology

Department of Human Development
Martha Van Rensselaer Hall
Ithaca, New York 14853-4401
t. 607.255.7620
f. 607.255.9856

July 16, 2008

Division of Behavioral and Cognitive Neurosciences
Directorate for Social, Behavioral and Economic Sciences
National Science Foundation
4201 Wilson Boulevard
Arlington, Virginia 22230-0002

Re: Matthew K. Belmonte
Applicant for CAREER award

Dear NSF Review Panel:

As a member of Dr. Belmonte's faculty mentoring committee in the Department of Human Development at Cornell, I am pleased to provide consultation and guidance on the management of graduate research assistants involved in his proposed research, as suggested in the review of his original CAREER application.

Graduate students play a critical role in faculty research at Cornell, as they do at any research university. The mentoring and management of graduate students are major responsibilities of all our faculty. My own experience in this regard during the past 20 years at Cornell, with additional experience gained as the director of graduate studies, department chair, and associate dean for research and graduate education in the College of Human Ecology, forms the basis of the guidance I will provide to Dr. Belmonte.

Dr. Belmonte is exceptionally well qualified to carry out the research described in his revised application, his plan is realistic, and his commitment to the project is unqualified. I look forward to working closely with him as a mentor and consultant.

Sincerely,

Steven S. Robertson
Professor
Department of Human Development
Cornell University
Ithaca, NY 14853

ssr4@cornell.edu

Cornell University
College of Human Ecology

Barbara L. Ganzel Ph.D.
Human Development
MVR Hall
Ithaca, NY 14853
t. 607.254.1629
f. 607.255.9856

July 14, 2008

Dear Dr Belmonte,

As you know, during my independently funded postdoctoral work in your laboratory this past academic year, I have been responsible for coordinating subject recruitment, scheduling and data management for your intramurally funded pilot studies. In cooperation with one graduate student pursuing his dissertation research and in shared supervision of several undergraduates responsible for behavioral testing, scoring, and data entry, I have served as the contact person for prospective subjects, disbursed subject payments, maintained subject records in secure storage, and set up the SPSS spreadsheet within which psychometric and behavioral scores are maintained and analyzed.

I look forward to continuing this work as part of your proposed NSF CAREER project "Integrative Behavioural and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments." The normative data from your studies will be an extremely valuable resource for my own work on MRI measures associated with normal cognitive variation.

Sincerely,

BL Ganzel

Barbara L. Ganzel, Ph.D.

Cornell University
Computing and Information Science

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July 17, 2008

Matthew Belmonte
Assistant Professor
Department of Human Development
G62A Martha Van Rensselaer Hall
Ithaca, NY 14853

Dear Dr. Belmonte:

The Game Design Initiative at Cornell would be pleased to continue participating in your research as part of your NSF CAREER project proposal "Integrative Behavioral and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments."

We will provide undergraduate students to continue development on the proposed video game, which provides an excellent source of undergraduate projects for us.

We look forward to continuing collaborations.

Sincerely,

Walker M. White
Faculty Advisor, The Game Design Initiative at Cornell

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Roger Sibley, *Executive Director*
C. Philip Meyer, M.D., *Medical Director*

Tompkins County Sites

☒ *Administration*
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Ithaca, NY 14850
Tel: 607.272.5891
Fax: 607.272.0188

❑ *Clinic*
1001 W. Seneca St.
Ithaca, NY 14850
Tel: 607.277.8020
Fax: 607.277.7961

❑ *TST BOCES*
555 Warren Rd.
Ithaca, NY 14850
Tel: 607.257.2353
Fax: 607.257.2510

Cortland County Sites

❑ 882 NYS Rt. 13
Cortland, NY 13045
Tel: 607.753.9375
Fax: 607.758.9287

❑ *OCM BOCES*
1710 NYS Route 13
Cortland, NY 13045
Tel: 607.758.5100
Fax: 607.753.9546

Tioga County Site

❑ 1277 Taylor Rd.
Owego, NY 13827
Tel: 607.687.8929
Fax: 607.687.8153

Website
www.rackercenters.org

July 11, 2008

Dr. Matthew Belmonte
Assistant Professor
Dept. of Human Development
Cornell University
G62A MVR Hall
Ithaca, New York, 14853-4401

Dear Dr. Belmonte:

As we discussed, I would be pleased to facilitate finding subjects for your project "Integrative Behavioral and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments." It is reasonable to expect that we can help you recruit up to twenty 10 - 15 year-old high-functioning children with autism spectrum disorders per year, who are capable of learning and playing the proposed video game. Recruitment can begin as soon as we receive a copy of the final IRB approval.

Sincerely,

Karen Fried, Psy.D.

Karen Fried, Psy.D.
Lic. #013775-1
Director of Autism Services
Licensed Psychologist

UNIVERSITY OF
ROCHESTER
MEDICAL CENTER

Rochester Center for Brain Imaging
PO Box 278917Rochester, NY 14627-8917

July 16, 2008

Matthew Belmonte
Department of Human Development, Cornell University
G62A Martha Van Rensselaer Hall, Ithaca, NY 14853-4401

RE: Letter of Support – Utilization of Research MRI facilities
Title: "CAREER: Integrative Behavioural and Neurophysiological Studies of Normal and Autistic Cognition Using Video Game Environments"

Dear Matthew:

In my role as Director of the Rochester Center for Brain Imaging (RCBI), I would like to assure you that the new 3T magnet and associated facilities at the RCBI will be fully accessible for you to acquire high resolution structural images as needed for your EEG work.

As you know, the RCBI houses a state-of-the-art whole-body 3T magnet (Siemens Trio). The center has a research agreement with the manufacturer to provide researchers with access to pulse sequence programming beyond standard protocols and access to on-going beta software packages. The RCBI also has a mock magnet that can be used to familiarize participants with the MR environment and train them to limit their head motion. The mock magnet setup mirrors that of the Trio as closely as possible, and in particular includes a surround sound system that reproduces the noises the Trio makes during a scan, and a motion feedback system that allows participants to learn how to reduce their motion. In addition to the facilities themselves, there is a staff of technicians, image analysts, and MR physicists to work with you. In particular, our MRI Technologist will be running the magnet and assisting your team with all aspects of data acquisition.

The goals and objectives of your grant application fit in well with the mission of the RCBI. The RCBI directorship is happy to support your project and guarantee that you will have access to the RCBI 3T facility for 24 subjects per year for each of the first four years (1 June to 31 May) of the proposal, with each subject needing one hour of scanner time. The RCBI functions as a service center and charges non-University of Rochester users a fee of $780.00/hour.

Sincerely,

Richard N. Aslin

Richard N. Aslin
William R. Kenan Professor
Brain and Cognitive Sciences
Director, Rochester Center for Brain Imaging