Defining and Quantifying the Social Phenotype in Autism

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Objective: Genetic and neurofunctional research in autism has highlighted the need for improved characterization of the core social disorder defining the broad spectrum of syndrome manifestations.

Method: This article reviews the advantages and limitations of current methods for the refinement and quantification of this highly heterogeneous social phenotype.

Results: The study of social visual pursuit by use of eye-tracking technology is offered as a paradigm for novel tools incorporating these requirements and as a research effort that builds on the emerging synergy of different branches of social neuroscience.

Conclusions: Advances in the area will require increased consideration of processes underlying experimental results and a closer approximation of experimental methods to the naturalistic demands inherent in real-life social situations.

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Autism is a neurodevelopmental disorder of early onset marked by a profound social disability affecting a person's capacity for understanding other people, intuiting their feelings, and establishing reciprocal relationships (1). Although several other developmental disabilities typically accompany autism's social dysfunction, including language and communication, learning, and unusual behavioral patterns, the core social disorder defines the condition and likely affects the development and expression of these other skills (2). However, despite its centrality in the syndrome's definition, a more precise characterization and quantification of the social dysfunction required to direct neurobiological research in autism is still lacking (3). For example, major advances in the genetics of autism have identified candidate susceptibility loci (4), but it is still unclear what indices of behavioral or cognitive features may correspond to the possibly discrete inherited vulnerabilities (5). Together with the notion of a broader phenotype of autism (6) and the pronounced heterogeneity in syndrome manifestation (7), different lines of research point to the need to refine the characterization of social dysfunction in autism to capture essential elements of sociability that may be disrupted, to differing degrees, in individuals with the prototypical, as well as the broader, manifestation of this condition (8). Similarly, despite the accumulating knowledge on brain structure and brain function in autism (9), replicable and quantitative connections between neuroimaging findings and behavioral or neuropsychological measures are still quite tentative (10, 11), particularly insofar as brain-behavior relationships in the social realm are concerned (3). This article briefly reviews more traditional attempts to quantify the social phenotype in autism and describes in detail novel, emerging methods of study.

Symptom-Based Approaches

One natural strategy to refine and quantify the phenotype in autism has been to develop more reliable behavioral measures of the symptoms characterizing the condition (12). Instruments such as the Autism Diagnostic Interview—Revised and the Autism Diagnostic Observation Schedule provide standardized diagnostic procedures. Such an approach is crucial in cross-site studies to ensure consistency of diagnostic procedures, e.g., for genetic studies. This approach, however, has important limitations. Symptom-based methods were created to produce cutoff points of discontinuity between individuals with autistic conditions and the general population. Modeling and quantifying continuously distributed characteristics, however, can be a more powerful approach to genetic analysis, reflecting the true state of nature rather than a reductive dichotomy of "affected" and "nonaffected" individuals. While symptom-based genetic analyses of some psychiatric disorders, such as obsessive-compulsive disorder (OCD), have born fruit (13), the mapping of normative tendencies or developmental processes (in the case of OCD, the need for symmetry and ordering) appear to correspond to a genetically significant subtype of OCD. Similarly, in the field of reading disabilities, genetic analyses using measures of normative skills, such as phonemic awareness (14), whose impairment appears to lead to the syndrome, rather than measures of the disability itself have shown more promise in capturing inheritable vulnerabilities.

Despite these limitations, however, symptom-based genetic research in autism has produced some preliminary successes. First, new attempts to capture the distribution of symptoms related to social processes, such as social reciprocity, have shown promise in creating a spectrum of results across varied populations (15). This was achieved

by defining social-reciprocity symptoms at different levels of severity, with autistic symptoms anchoring the more "affected" end of the scale. Second, deficits in social communication or pragmatics (16) have identified immediate family members of probands with autism relative to normal comparison subjects. This and similar methods do, therefore, hold the potential for the creation of a continuum of "affectedness" that could be helpful in measuring the broader spectrum of autism, although this has not yet been attempted. The limitation of such methods hinges on the fact that communication failures are likely to result from the intersection of very complex developmental and other processes, greatly complicating the effort to map them genetically or neurofunctionally.

Approaches Based on Normative Developmental Processes Not Specific to Social Functioning

The search for developmental processes whose derailment could represent core (i.e., causative) deficits in autism—perceptual, neuropsychological, or behavioral—have historically focused on general processes not specific to social functioning but those that were thought to underlie socialization deficits in individuals with autism (17). Studies of attentional abnormalities (18), perceptual dysregulation (19), and language functions (20), among many other areas of psychological functioning, have made important contributions to the characterization of a range of disabilities accompanying the core social disorder in autism. It is unknown, however, whether there is a proportional relationship between deficits in such functions and degree of social dysfunction evidenced in autism (e.g., more perceptual dysregulation predicts a greater degree of social dysfunction). One notable exception has been the study of language functions in autism (20), in which studies have repeatedly shown that degree of language impairment is highly correlated with degree of social dysfunction. However, both of these are also highly correlated with IQ, which remains one of the best predictors of social outcome in autism. Neither language nor IQ, however, can be used to predict degree of social dysfunction in the entire spectrum of autism. Between one-fourth and one-third of the individuals with autism-related conditions have IQs in the normative range or above (21) and relatively adequate, formal language capacities (i.e., excluding prosodic and pragmatic skills); however, they have profound social disabilities. From a genetic standpoint, despite the fact that a majority of individuals with autism exhibit mental retardation and language disabilities, neither language nor IQ deficits (8) have been shown to aggregate in family members of these individuals in a way that separates these families from the families of individuals with other conditions.

Two more recent hypotheses of social dysfunction based on more generalized psychological functions deserve special attention. First, an impressive number of studies have documented deficits in executive functions in individuals with autism of all ages and intellectual levels (22). "Executive functions" refers to a group of neuropsychological skills that allow a person to maintain an appropriate problem-solving set in order to attain a goal. Among the various constructs subsumed under executive functions, planning—and particularly flexibility or set-shifting—are thought to be the skills most affected in autism (22). This hypothesis has great face validity, given that individuals with autism are known, for example, to perseverate on inappropriate responses and to have great difficulty planning and organizing their daily affairs. Abnormalities in the brain circuitry subserving executive functions, particularly the dorsolateral-prefrontal cortex, are thought to give rise to the social dysfunction in autism (23). There are several challenges to this hypothesis, however, including findings that deficits in executive functions are seen in a number of other disorders (23) and that such deficits may not be correlated with degree of social disability (24). Nevertheless, a small number of studies have already shown differential aggregation of deficits in executive functions in parents (25) and in siblings (26) of autistic probands.

The second hypothesis refers to the construct of weak central coherence, which is thought to capture the lessened neuropsychological tendency of individuals with autism to integrate information into a coherent or meaningful whole (27). Even though the supportive literature is still limited (28), the construct is very appealing because it captures the characteristic learning style seen in autism, which is marked by attention to fragmented and isolated aspects of the environment to the neglect of contextual and overall meaning. Like the executive-functions hypothesis, however, the focus of researchers in weak central coherence has been the documentation of deficits of weak central coherence in individuals with autism relative to comparison subjects, with little attempt as yet to substantiate the distinct association between weak central coherence and social disorder or to provide a developmental and neurofunctional account of the hypothesized drive for coherence. Nevertheless, the potential presented by this line of research is great, given that a drive for configural processing, going from parts to meaningful wholes, is likely to be present from very early in life—e.g., when visual stimuli become human faces with specific affective attitudes—and is likely to remain central throughout the lifespan (29).

Approaches Based on Normative Developmental Processes Specific to Social Functioning

The past two decades of research in autism have evidenced a shift in focus to direct studies of social dysfunction based on normative socialization processes. Among these, a great deal of attention has concentrated on studies of face perception (30). This line of research is impor-

tant, given the central role attributed to face perception in the process of socialization. Although it seems relatively clear that young and more cognitively disabled children with autism show face-perception deficits relative to mental-age-matched comparison subjects (31), the effect size of such findings is much lower in older and more cognitively able subjects (32). Of interest, however, abnormalities in processing, rather than deficits in performance, have been more consistently reported, including lack of "inverse effect" (33) and a tendency toward featural rather than configural processing of facial stimuli (34). Individuals with autism do not show a normative decrement in performance when matching upside-down faces compared to their performance when matching right-side-up faces; they seem to rely on parts of the face rather than the whole image when performing face-recognition tasks. These findings have highlighted the need to focus not only on results but also on the ways in which individuals with autism perform face-perception tasks and the developmental considerations necessary to interpret performance results. For example, there is some indication that rather than representing a face-specific deficit of a presumably neurofunctional region (e.g., a structural abnormality of the "face area" of the brain, which is thought to be the fusiform gyrus), abnormalities in autism may reflect a lack of expertise with facial stimuli by autistic individuals (34) (e.g., as social stimuli). This would then probably reflect a lack of repeated exposure to such stimuli early in life due to the person's history of social disengagement or, in other words, due to the person's autism (35). This would not diminish the utility of measures of face perception as quantified indicators of social disability if a relationship with general social dysfunction could be identified, although this has not yet been done. To our knowledge, face-perception methods have not yet been used in genetic research in autism. Nevertheless, there are strong neurofunctional models of face-processing skills in typical (36), brain-injured (37), and autistic populations (11, 30), raising the possibility that the definition of a neurofunctional social "endophenotype" is on the horizon.

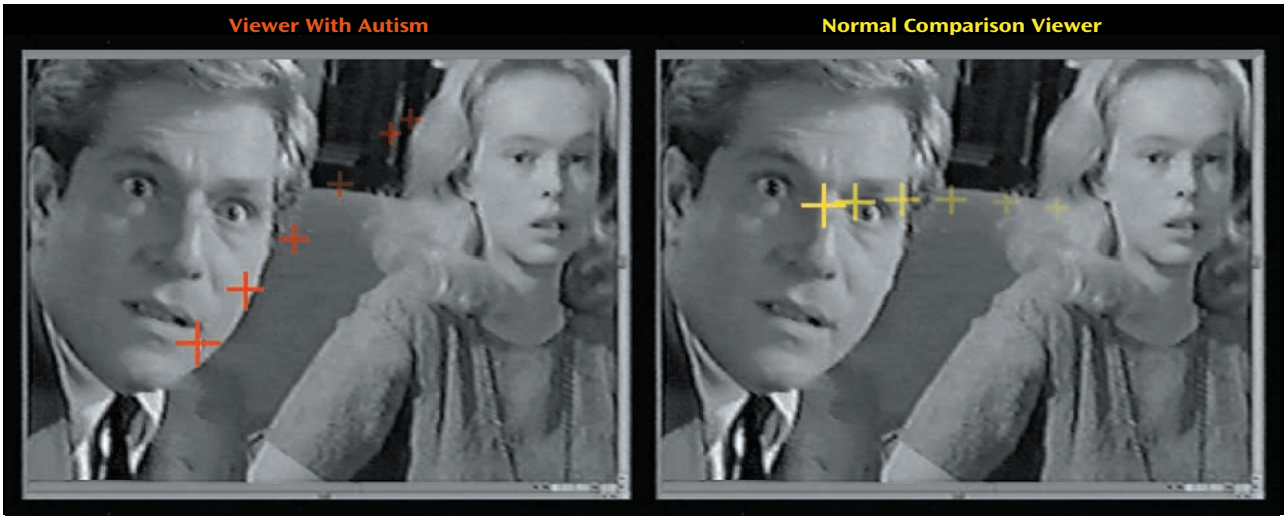
The most influential construct currently used to refine the characterization of the social phenotype in autism is the theory-of-mind hypothesis of interpersonal understanding (38). This model of social development posits that being able to conceive of mental phenomena, in others as well as oneself, is the foundational mechanism making possible intersubjectivity. Individuals with autism are thought to be unable to think of other people in terms of mental states, such as beliefs, intentions, desires, and feelings, and are unable to use this knowledge to explain and predict another person's behavior. The consequences of this incapacity for mentalizing about others are thought to be far-reaching (39). To interact with others without the implicit understanding that their behavior is inextricably connected to their intentions, beliefs, and feelings is to focus exclusively on the literal meaning of their language and acts. This results in sweeping neglect of why specific language and acts are used in the ways they are, as well as neglect of a host of implied meanings that define the context of the social interaction.

In the past few years, however, a number of limitations to the explanatory power of the theory of mind have been raised. These include the lack of specificity of theory-of-mind findings to autism (40, 41), as well as the strong relationship between the theory of mind and language abilities (41). The most intriguing limitation, however, has emerged from studies of cognitively able individuals with autism. Despite their pronounced social disability, these individuals have been shown to succeed in performing theory-of-mind tasks at different levels of complexity, and, in some situations, they are certainly capable of conversing with others about mental states (42, 43). However, these skills do not translate into commensurate social competence in naturalistic environments (35), and successful attempts to teach theory-of-mind skills in a therapeutic program have not translated into improved social or communicative competence (44). The relative success of cognitively able individuals with autism in the performance of theory-of-mind tasks seems to result from a series of factors that may foster task performance on experimental tasks but not facilitate social adaptation in real life (45). First, by reducing the number of confounding variables in order to focus attention more directly on the underlying mechanism, experimental tasks may inadvertently render social understanding an explicit problem-solving situation, whereas real-life social situations are typically dependent upon creating context through correct interpretation of implied cues. Second, theory-of-mind tasks are usually verbally mediated, whereas communication demands in real-life social situations often depend upon nonverbal social cues, which both create context and modify the literal meaning of language. Third, traditional theory-of-mind tasks are not sensitive to the less profound social disabilities exhibited by higher-functioning individuals. However, several more advanced theory-of-mind tasks have been shown to capture more subtle theory-of-mind deficits in less disabled autistic populations (46, 47). In general, therefore, theory-of-mind measures remain one of the central candidates for better characterization of the social phenotype in autism. Their utility will improve further with better quantification of the construct, a shift from a categorical to a dimensional approach, and greater attention to the ecological validity of theory-of-mind research methodology. Although genetic studies of theory-of-mind abilities are still lacking, an emerging neurofunctional literature has already delineated viable brain models of mentalizing capacities (10).

The Need for Novel Methods

As shown in this review, a number of promising constructs and methodologies are available for the quantifica-

FIGURE 1. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip Containing the Face of a Shocked Young Man



tion of the varied manifestations of the autistic social phenotype. Approaches emphasizing the derailment of normative processes that can be measured continuously and that directly, or by association, can model variable social dysfunction are more likely to map on genes and on brain function. Several challenges to current methods remain, however, outlining future programmatic efforts in this field of research. First, there is a need for better substantiation of the relationship between generalized neuropsychological constructs and social disability. The assumption that such processes are more basic and, therefore, underlie and are relatively independent of social development often goes unchecked. However, there is evidence to suggest that deficits in at least some neuropsychological functions vary as a result of how socially demanding a given task is (48). Similarly, the possibility that profoundly abnormal social experiences with onset in the first year of life may affect specific neuropsychological as well as brain processes, rather than the other way around, is typically not discussed or studied (35). For example, the possibility that early social engagement may play an important role in facilitating a child's drive for coherence of experiences and for flexibility in dealing with the world is a worthy topic of inquiry, since most current models of brain development view the brain as a repository of experiences just as much as a determining factor in the unfolding of innate capacities (49).

The second research challenge has to do with the need for a shift of emphasis from results on task performance to processes used by individuals with autism to perform a given task. This was made clear in a recent study showing decreased fusiform and increased inferior temporal gyrus activation in a group of individuals with autism who were performing a face-recognition task (34). From a brain-activation perspective, these individuals treated faces as objects. However, from a behavioral perspective, their performance on the task was as accurate as that of the comparison group. Evidence for compensatory strategies in task performance abounds in the experimental literature of autism, particularly in individuals with considerable cognitive and language strengths; thus, processes underlying performance results may have to be manipulated for this issue to be properly addressed (50).

The third challenge concerns the fact that a number of factors artificially inflate the performance of individuals with autism on experimental tasks. If we are to model their difficulties in social adaptation, there is a need to neutralize scaffolding factors through the creation of novel methods capable of recreating in the laboratory the more demanding aspects posed by naturalistic social situations. Despite three decades of experimentation, the most obvious indication of the profound social disability witnessed in autism is still the spontaneous presentation of affected individuals in unstructured social interaction. Laboratory approximations of such conditions are likely to increase the effect size and power of research procedures. This was exemplified in a recent theory-of-mind study focused on the spontaneous tendency of cognitively able individuals with autism to impose social meaning on ambiguous visual stimuli (45). The subjects viewed a classic silent cartoon in which social situations were enacted by geometric shapes. While comparison subjects immediately appreciated the social nature of the action, naturally anthropomorphizing the shapes through attributions of intentions, beliefs, and feelings to them, the individuals with autism failed to do so. While, on average, they were able to identify only one-fourth of the social elements of the cartoon relative to the comparison subjects, a considerable number restricted their narratives to physical or geometric, not social, attributions. Given that all of the autistic individuals had successfully performed a relatively advanced but more traditional theory-of-mind task, this study showed

FIGURE 2. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip of a Conversation

the utility of measuring spontaneous responses in a nonexplicit, nonverbal setting.

A Novel Paradigm for the Social Phenotype in Autism

In order to better capture, characterize, and measure the profound social dysfunction evidenced in naturalistic contact with persons with autism, we recently began to use eye-tracking technology to study their spontaneous viewing patterns when presented with real-life social scenes. This method allows the investigator to see the world through the eyes of an individual with autism. Precise measurements of the subject's visual focus are superimposed over the dynamic images of viewed film clips. The resultant videotape can then be analyzed and coded for a detailed characterization of viewing patterns. The potential of this paradigm is exemplified in a number of illustrations we obtained by contrasting discrete viewing instances of one cognitively able (full-scale IQ=119) male adult with autism and an age, gender, and IQ-matched comparison subject with typical development. The moment-by-moment visual traces left behind by the saccadic movements and fixations of the individual with autism appear to represent quite vividly his atypical attempts to create social meaning out of what he saw. The two individuals watched digitized clips of the film version of Edward Albee's classic *Who's Afraid of Virginia Woolf*? This movie was chosen because it displays the intense interaction of four protagonists involved in a content-rich social situation likely to maximize viewers' monitoring of each person's socially expressive actions as well as those characters' reactions to the actions of others. The demanding social complexity in the movie was intended to mirror complicated social situations that individuals with autism may encounter in their everyday social life, such as at a school dance or at lunch in a cafeteria.

Looking at Faces

In real-life social situations, many crucial social cues occur very rapidly. Failure to notice them may lead to a general failure to assess the meaning of entire situations, thus precluding adaptive reactions to them. This is exemplified in Figure 1, which shows a still image of two of the film's characters: at left, a young man, Nick, and at right, his wife Honey. Overlaid on the image are crosses that mark, in red, the focus of the viewer with autism and, in yellow, the focus of the normal comparison viewer. The boldest crosses mark each viewer's visual focus while watching the film; the gradational crosses reveal the direction from which the viewers' visual focus traveled. While viewing the previous film shot, both viewers were focused on the right half

FIGURE 3. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip of a Silent Actor

of the frame. An abrupt change in camera angle occurred, and both viewers responded immediately. While the normal comparison viewer responded directly to the look of surprise and horror in the young man's wide eyes, the viewer with autism tried to gather information from his mouth. Nick's mouth is slightly open but quite expressionless, and it provides few clues about what is happening in the scene.

Although previous literature has documented greater reliance on mouths rather than eyes when participants with autism are required to perform face-perception tasks (33, 51) and have difficulty "reading" the meaning of eye expressions (46), our findings present a starker documentation of these tendencies. Figure 2 shows 2 seconds of eye-tracking data superimposed onto one still image from a scene involving heated dialogue between the film's two other main characters, Martha and George. While the normal comparison viewer's visual focus (in yellow) shifted from eye to eye, the focus of the viewer with autism (in red) shifted from mouth to mouth and across adjacent regions.

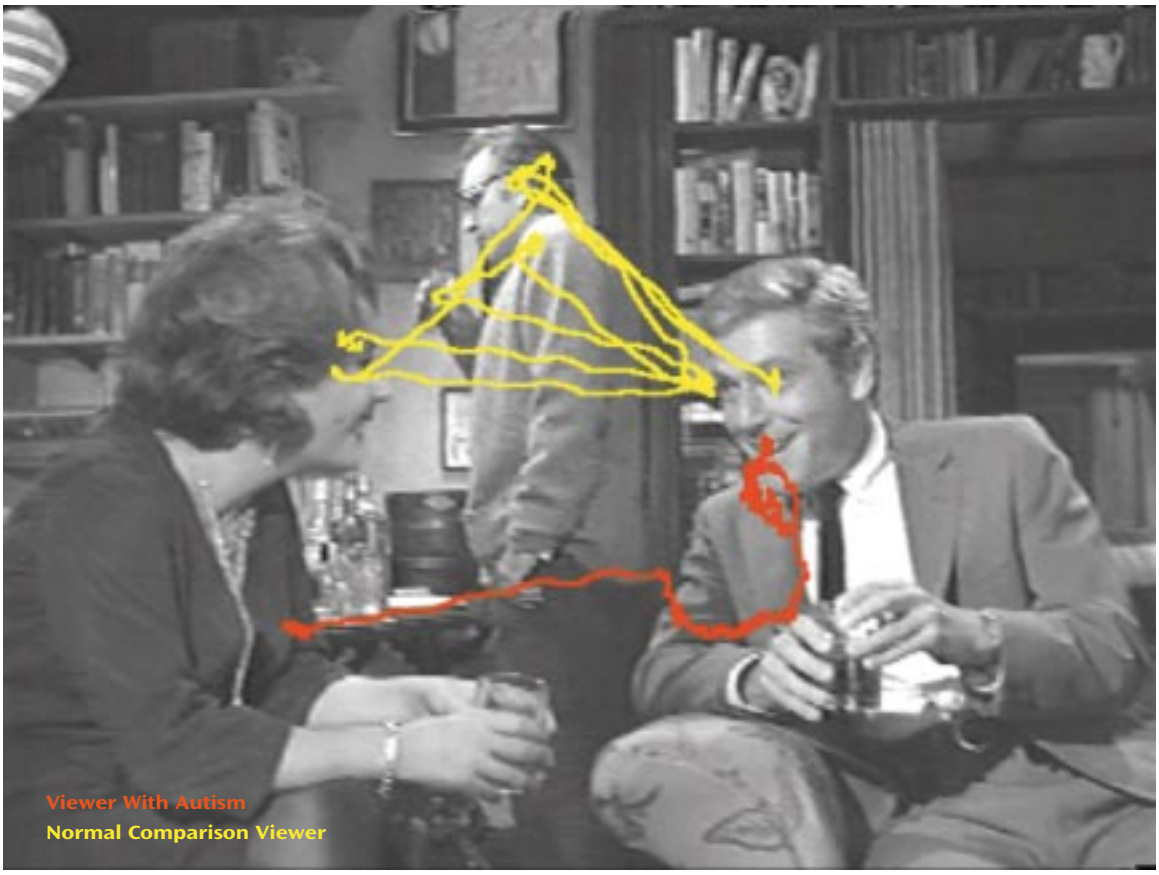
The persistence with which the viewer with autism sought visual information in the mouth regions of the actors is further exemplified in Figure 3, from a scene in which all of the actors were silent for more than 13 seconds. This figure shows eye-tracking data from this silent episode collapsed onto one still image. As shown, the viewer with autism (in red) continued to focus entirely on the mouth and lower portion of the face, whereas the normal comparison viewer (in yellow) focused primarily on the eye region. Although no words are exchanged during this scene, the uneasy and growing silence that results from the protagonists' discomfort in being together is meaningfully expressed in the actress's facial expression, particularly in her gaze.

Social Monitoring

Adequate interpretation of social situations often requires searching for social information in others' reactions to the speaker. For example, ironic or embarrassing remarks are likely to produce reactions in listeners that help a viewer make sense of the social dynamics determining the unfolding context of the conversation. Failure to do so may result in a very partial, overly literal, or mistaken interpretation of a social situation. This is exemplified in Figure 4, which shows eight still images in the midst of a 13-second conversation in which the young man, Nick, initially speaks to a listener, while his young wife Honey reacts to what he said (frames 1 and 2). Thereafter, Honey speaks to the same listener while Nick reacts to what she said (frames 3 through 8). As shown in this figure, the viewer with autism (red crosses) focused almost solely on

FIGURE 4. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip Portraying an Embarrassed Nonspeaker in a Social Situation

FIGURE 5. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip Portraying a Flirtatious Exchange



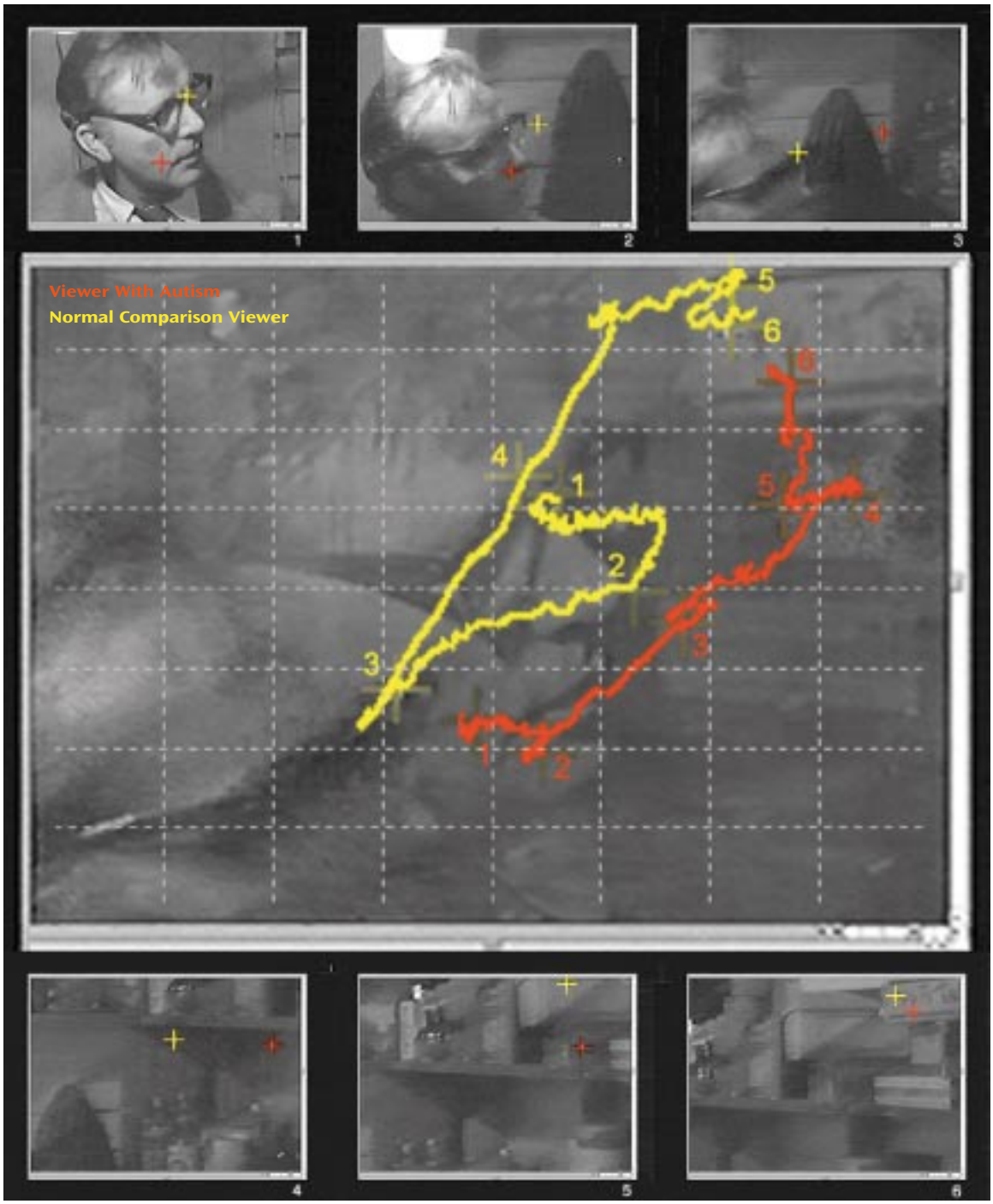
the speakers' mouths, staying with Nick for the first two frames and then moving to, and remaining focused on, the mouth of the young woman for the next six frames. He did not monitor the reactions of the nonspeaker. However, shifting focus in frames 3, 4, 6, and 8 is critical for understanding the mood of this scene. In these frames, monitoring Nick reveals the impact of his wife's words on his emotional state. In frames 3 and 4, Nick's avoidant, downcast eyes show his discomfort and uneasiness in response to the story she is telling. In frame 6, Nick turns to the conversational partners, facing them with a wry and embarrassed grin. Finally, in frame 8, he resignedly turns back toward his wife. These reactions (his grudging, reluctant acceptance of her storytelling and how this ultimately reflects his embarrassment with her and the way she is acting) tell far more about the relationship of these two people and the meaning of this scene than the actual story Honey is telling. If we follow the eye-tracking path of the viewer with autism, it is very likely that he was unaware of much of the social meaning contained in these frames. In marked contrast, over the course of the 13-second clip shown in Figure 4, the normal comparison viewer (yellow crosses) shifted focus six times, compared to one shift on the part of the viewer with autism (red crosses).

Figure 5 displays another instance when an appreciation of the way in which the speakers are conversing, rather than of what they are saying, is crucial to understanding the meaning of the social scenario. In the foreground, Nick and Martha lean into a flirtatious exchange, while standing in the back, fully aware of all they are doing and saying, is her husband George. Figure 5 shows the visual scanning paths of the two participants during this 7-second shot. The data are shown collapsed onto one still image. From the scanning pattern in this figure, the viewer with autism (red path) seemed not to understand the inviting, flirtatious nature of the interaction—or the impact of these behaviors on Martha's husband in the back, since he did not once glance at the action in the background. In contrast, the normal comparison viewer's visual scanning delineated a rather loaded social triangle.

Negotiating Physical Versus Social Cues

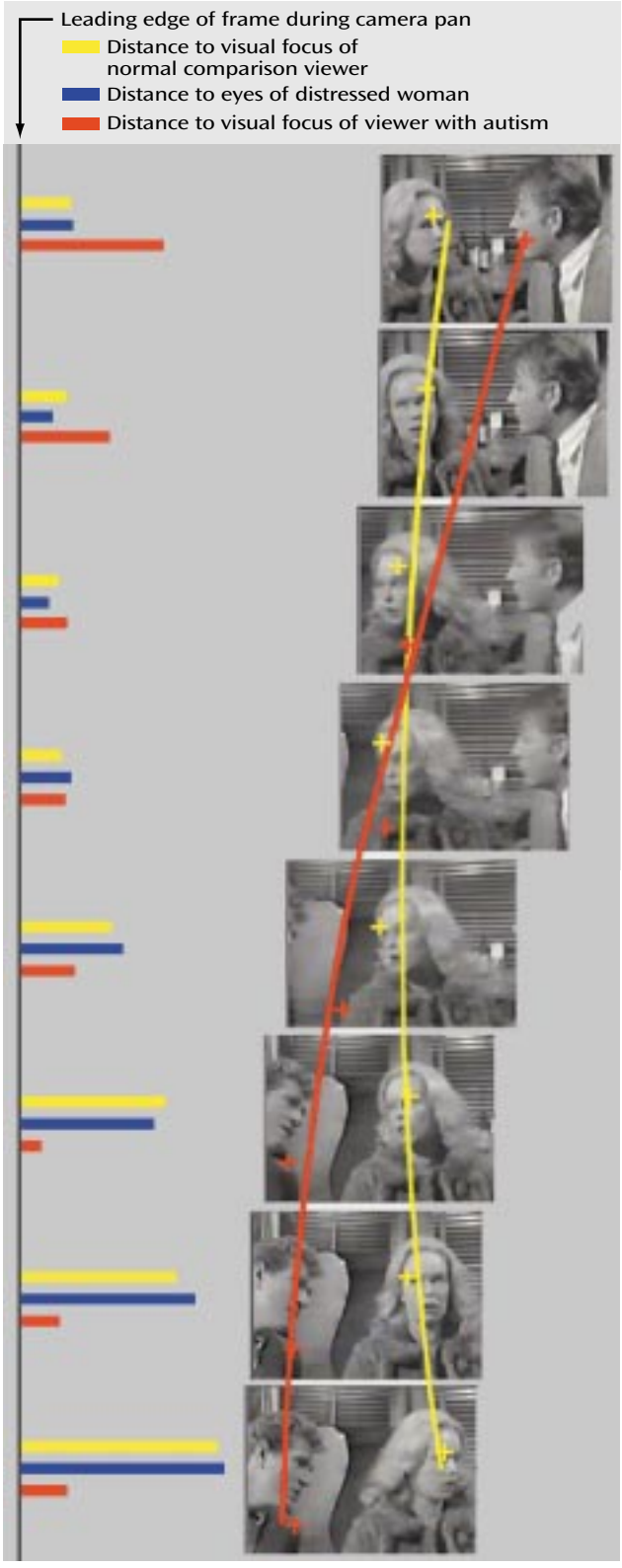
In order to examine whether the viewer with autism had lower sensitivity to social cues, and not to visual cues in general, we selected a scene in which there was no social interaction but important physical cues affecting visual pursuit. This scene takes place inside a small storage room and shows George reaching for a gun that is wrapped in a piece of cloth and resting on the upper shelf of the storage

FIGURE 6. Visual Focus of an Autistic Man and a Normal Comparison Subject Shown a Film Clip With Physical Attentional Cues



cabinet. Figure 6 shows six frames from a 2.5-second camera pan to the right. By physically shifting the field of view, the camera pan indicates that important information will soon be seen at the right edge of the screen. As the camera begins to pan, both viewers at first maintained a visual focus roughly centered on the image of George. When we traced the movement of each viewer's visual focus, the graph at the center of the figure shows that the viewer with autism responded to this physical attentional cue more quickly than the normal comparison viewer. His visual focus, in fact, moved faster than the camera itself, attesting to his clear understanding of, and quick response to, the physical cue. The normal comparison viewer's visual tracing, however, showed a small but important difference. Overall, his visual scanning pattern showed an equally fast reaction to the physical cue, but, as shown in the graph, his visual pathway was not as straightforward as that of the viewer with autism. Before his focus moved completely to

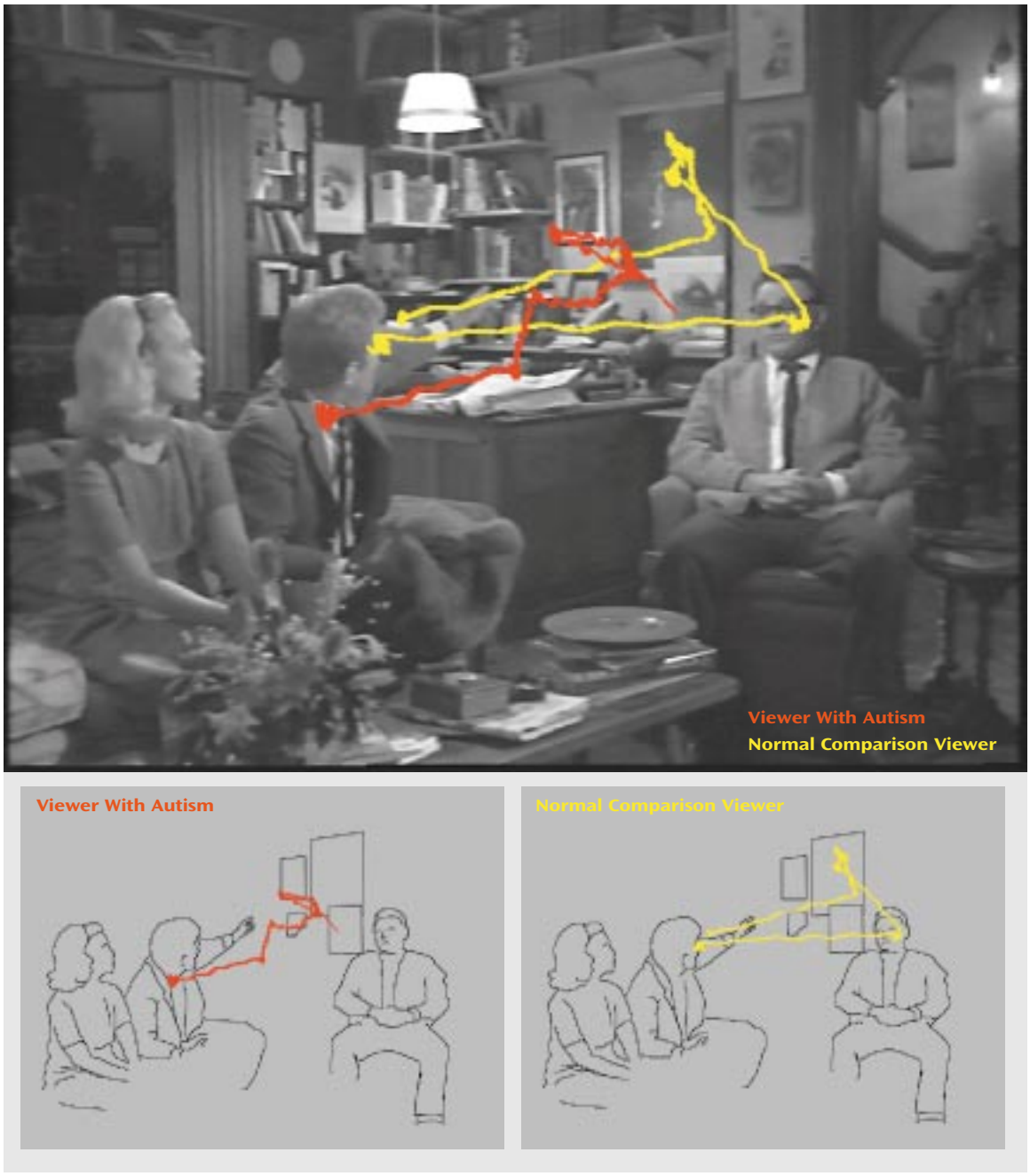
FIGURE 7. Visual Focus of an Autistic Man and a Normal Comparison Subject Relative to Social Cues in a Film Clip and the Camera's Physical Motion



the right, it pulled back in the direction of George, possibly seeking additional information about his intentions. This tension between the physical and social cues, manifested in a looping, back-and-forth pattern, was not seen in the visual tracing of the viewer with autism. This suggests that the two viewers reacted to the physical and social cues differently, guided by relative levels of salience: the viewer with autism disregarded the social cues, whereas the normal comparison viewer was momentarily distracted by them.

Most situations in real life contain physical and social cues. For example, a school cafeteria may be filled with children communicating and playing with one another, but it also contains furniture, light fixtures, pictures on the wall, and the like. To concentrate on important social demands, there is a need to relegate these physical elements to the background of one's attention until they become relevant in a given situation. Given the small number of studies suggesting that individuals with autism display greater orientation to objects than to people (52, 53), we explored further the tension resulting from physical and social cues occurring together. A film clip was selected in which there is a strong physical cue resulting from camera movement and an equally strong social cue in the form of dramatic facial expressions made by the actors. In this scene, George (at right) has just revealed a painful and embarrassing secret about the young woman, Honey, that he had previously heard from her husband Nick (at left). Figure 7 shows this scene just after George has divulged the secret, as Honey turns incredulously back and forth between the two men. George has a rather cruel, sarcastic expression as the young woman reacts wildly to the revelation. Nick is greatly dismayed and aims a pleading look of both anger toward George and a look of repentance toward his wife. Figure 7 shows the focal point of both viewers in relation to the emotional reactions of the actors and the physical motion of the camera. At the moment that Honey hears the revelation and begins to react in a dramatic display of hurtful emotions, the camera immediately pans to the left, although Nick is not yet visible. As shown, the viewer with autism (red crosses), who had previously focused solely on the mouths of George and the young woman, was sensitive to the physical (camera) cue and moved quickly to the left without glancing at Honey's eyes and much before Nick becomes visible in the scene. Plotting the movement of his visual focus across the images shows how the focus of the viewer with autism followed the leading edge of the camera and not the social-emotional turmoil of the characters—a point made clear by the fact that the viewer with autism never even looked at Nick's face, focusing instead on his shoulder. In marked contrast, the normal comparison viewer's eyes were "glued" to the woman's emotional facial displays as her head moves back and forth (yellow crosses), disregarding the initial camera shift to the left in favor of the more salient displays of emotion. The way in which the two viewers negotiated the social and the physical cues in their selective visual attention was, therefore, markedly different.

FIGURE 8. Visual Scanning Patterns of an Autistic Man and a Normal Comparison Subject Shown a Film Clip With Social-Visual and Verbal Cues



Sensitivity to Nonverbal Social Cues

Nonverbal social cues can both modify and further specify what is said. For effective communication exchange, verbal and nonverbal cues need to be quickly integrated. Figure 8 shows a scene in which Nick inquires about a painting hanging on a distant wall. In doing so, he first points to a specific painting on the wall and then asks George (who lives in the house), "Who did the painting?" While the verbal request is more general (since there are several pictures on the wall), the act of pointing has already specified the painting in which the young man is interested. The figure shows the visual scanning paths of the viewer with autism (in red) and the normal comparison viewer (in yellow). As shown in Figure 8, the viewer with autism did not follow the pointing gesture but instead waited until he heard the question and then appeared to move from picture to picture without knowing which one the conversation was about. The normal comparison viewer (in yellow) followed Nick's pointing finger immediately, ending up, very deliberately, on the correct (large) picture. After hearing the question, he then looked to George for a reply and back to Nick for his reaction. The vi-

sual path he followed clearly illustrates his ability to use the nonverbal gesture to immediately inspect the painting referenced by the young man. In contrast, the viewer with autism used primarily the verbal cue, neglecting the nonverbal gesture and, in doing so, resorted to a much more inefficient pursuit of the referenced painting. This illustration also demonstrates the discrepancy between what this person with autism knew explicitly and what he did spontaneously. He was later questioned, in an explicit fashion, about whether he knew what the pointing gesture meant. He had no difficulty defining the meaning of the gesture; however, he did not use this explicit knowledge when viewing the scene.

Collectively, these visual tracings bring to the fore a number of processes potentially underlying the very limited capacity for social adaptation exhibited by individuals with autism. A pronounced focus on mouths rather than eyes, neglect of crucial social and communicative cues, and preferential attention to physical over social cues are likely to be but a fraction of the underlying factors leading to their social dysfunction in such settings. The challenge remains, however, to quantify these complex atypical responses so that discrete processes can be studied under more constrained conditions.

We recently made a step in that direction by greatly simplifying these questions to render them more viable. We collected eye-tracking data for spontaneous viewing patterns to the same digitized film clips for cognitively able adolescents and young adults with autism and age- and verbal-IQ-matched comparison subjects with typical development (54). We studied the relative salience of major components of the viewed scenes by dividing the total on-screen area into a face area (eye and mouth regions), a body region, and an inanimate object region. A comparison across the two groups revealed marked differences. Individuals with autism focused twice as much time on the mouth region of the faces, 2½ times less on the eye region of the faces, and 2½ times more on the body and object regions than did the normal comparison subjects. The best predictor of membership in the autism group was the measure of time of visual fixation on the eyes; there was no overlap in the distribution of results across the two groups. These findings supported the indications obtained in the current single-case observations. Given the fact that preferential attention to eyes rather than mouths (55) and for social rather than inanimate objects (56) are viewing patterns established in the first year of life, these results suggest that despite their considerable cognitive and language skills, this group of individuals with autism evidenced a robust abnormality in the social skills that normatively emerge in early infancy. Of special interest, measures of viewing patterns were related to outcome measures of social competence. There was a strong positive correlation between viewing time focused on mouths (but not on eyes) and social competence; i.e., the more the participants focused on mouths, the more socially competent they were. This result raised the possibility that by focusing on mouths these individuals with autism might attain some understanding of social situations (perhaps because of greater, focused attention on speech), whereas attention to eyes may not lead to any additional social insights. There was also a strong negative correlation between time viewing objects and social competence; i.e., the more the participants focused on objects, the less socially competent they were. This result raised the possibility that by focusing on objects these individuals might be neglecting to focus on any stimuli of social significance, faces, or speech.

Although it greatly simplifies the complexity of general social viewing patterns, this methodology seems to provide a new inroad into the social phenotype in autism, providing quantification of social phenomena that have hitherto been primarily observed only in clinical settings. The utility of building on an experimental design that more closely resembles naturalistic social demands was suggested by the correlations obtained between measures of viewing patterns and outcome measures of social competence. We are currently examining whether this method might prove equally effective in quantifying social disability in a broader range of manifestations of autism—in terms of age, cognitive level, and degree of severity of the condition.

Future Directions

Improvements of quantification methods for measuring the social phenotype in autism are likely to require more sensitive experimental techniques that recreate in the laboratory the natural demands of real-life experiences. Eye-tracking studies of social visual pursuit represent a promising new line of research, although their potential is still largely untapped. Some of the phenomena illustrated correspond to social skills normally acquired in early infancy. There is the opportunity, therefore, for methodological adaptations that will make possible prospective measurements of social visual pursuit from the time infants are identified as at risk of having autism, thus allowing us to examine the onset and natural course of this construct, as well as to measure its predictive value regarding eventual outcome. Such adaptations could also help us probe the hypothesis that similar vulnerabilities are found in family members, including siblings born subsequently to the affected child. Studies of this nature might elucidate the question of whether the correspondence between quantified abnormalities in social visual pursuit and outcome measures of social competence in the broad range of autistic manifestations is continuous (along a dimensional spectrum) or maps on clinically significant discontinuities.

One of the exciting aspects of this line of research is the opportunity that the construct of social visual pursuit presents for research integrating behavioral, neurofunctional, and comparative methodologies. Because skills such as

preferential sensitivity to salient social stimuli (e.g., conspecifics versus inanimate objects, eyes versus mouth) are likely to map on fairly conserved brain functions (11, 57, 58), there is potential for great synergy between eye-tracking behavioral studies, functional neuroimaging studies, and animal models. In the area of social visual pursuit, as in the areas of mentalizing and neuropsychological studies, there is now the potential for constraining and testing hypotheses simultaneously at these various levels of research. This concerted effort holds the promise, therefore, of not only contributing to a refinement of our views of the social phenotype in autism but also of unraveling central aspects of the pathogenesis of this and related conditions.

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Donald Cohen, M.D., died in 2001. This article is dedicated to the memory of the authors' mentor, collaborator, and colleague, whose legacy embodies the best in clinical services, public advocacy, clinical science, bioethics, and mentoring.

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