

eMethods. Additional Information on Exclusion Criteria, Measures, and Statistical Analyses

Participants

Potential participants were excluded for the following reasons: child not fluent in English, MRI contraindication (e.g., irremovable ferromagnetic implants or dental appliances, claustrophobia, pregnant), major neurological disorder, gestational age less than 28 weeks or birthweight less than 1,200 grams, history of traumatic brain injury, or had a current diagnosis of schizophrenia, autism spectrum disorder (moderate, severe), mental retardation/intellectual disability, or alcohol/substance use disorder.

Study Investigators and Sites

The participating sites are listed below and a complete listing of the study investigators can be found at <https://abcdstudy.org/principal-investigators.html>.

Children's Hospital Los Angeles
Florida International University
Laureate Institute for Brain Research
Medical University of South Carolina
Oregon Health & Science University
SRI International
University of California Los Angeles
University of California San Diego
University of Colorado Boulder
University of Florida
University of Maryland at Baltimore
University of Michigan
University of Minnesota
University of Pittsburgh
University of Rochester
University of Utah
University of Wisconsin-Milwaukee
University of Vermont
Virginia Commonwealth University
Washington University, St. Louis
Yale University

Measures

Prodromal Questionnaire-Brief Version (PQ-BC)

PQ-BC Scale Creation. Approximately five 10-12-years-old participants with chromosome 22q11.2 deletion syndrome responded to a pilot test of the original PQ-B. The PQ-B has a Flesch-Kincaid reading grade level of 7.5 and had not been used in studies with children under age 12 previously. Many items included language that was too abstract for their comprehension, and consequently, after reading each item to participants the clinician (Ingrid Leckliter) also routinely explained the items orally. This difficulty with comprehension led the PI (Tony Simon) and Ingrid Leckliter from the UC Davis MIND Institute 22q11.2 Research Center and Clinic to modify the wording of the items to be more developmentally appropriate for children. With the aim of improving participants' understanding, Tony Simon, Ingrid Leckliter, and other collaborators revised and reviewed approximately 6 drafts of the PQ-BC. As the iterations progressed, Ingrid Leckliter piloted the PQ-BC items with approximately 7 more participants. Several cartoon figures were piloted for the PQ-BC, including various black-and-white, line-drawn cartoon figures (e.g., thermometers, scared cat, boy, girl). However, 9-to-10-year old children did not grasp the abstract concept of using thermometers to rate distress, and furthermore, found the figures of the cat to be distressing. Therefore, investigators used the human figures for the distress rating scale. Given limitations on time to start the study and child burden, as well as the potentially adverse impact that repeating the same instrument can have on cooperation, no youth responded to both the original PQ-B and the version modified for children. Lastly, twelve ABCD sites also piloted a protocol that included the PQ-BC with a total of 52 participants, ranging in age from 7 to 11 (86.7% aged 9-10-years-old).

PQ-BC Scale Information. The PQ-B shows good internal reliability^{1,2} and convergent validity with clinician-measured assessment of psychosis risk.^{3,4} All PQ-BC questions were read to participants by research assistants, in accordance with the ABCD protocol to read all measures to participants to facilitate participants' comprehension of each item. Children first answered each question either yes or no. For each "yes", children were instructed to answer the follow-up question, "Did it bother you?". For each "yes", children were subsequently asked: "Please choose the number below the appropriate picture that shows us how much that bothered you when it happened.", with the numbers corresponding to the pictures ranging from 1 to 5 (see eFigure 1 for the pictures; the inclusion of pictures to assist in rating distress is a modification from the PQ-B, in which participants were asked to rate distress from 1=strongly disagree to 5=strongly agree). Missing data were coded as nos.³

In addition, a significant distress score was calculated, a summation of the number of endorsed questions rated on the distress scale from 3-5 (i.e., 0=no, 1=yes with a rating on the distress scale from 3-5). Significant distress score results are reported when deviating from other reported results. The PQ-BC measure is included in the Supplemental material.

Internalizing and Externalizing Symptom Measures

There is a wealth of evidence for the reliability and validity of the KSADS as a measure of psychopathology for children and adolescents.⁵⁻⁸ The depression symptom module showed good internal reliability (child-rated: $\alpha=.843$; parent-rated: $\alpha=.844$). The Generalized Anxiety Disorder (GAD) symptom module also showed good internal reliability (child-rated: $\alpha=.855$; parent-rated: $\alpha=.974$). Lastly, the bipolar symptoms module showed acceptable internal reliability (child-rated: $\alpha=.835$; parent-rated: $\alpha=.742$).

Child-rated externalizing symptoms were assessed with the UPPS-P for Children Short Form (UPPS-P-CSF; ABCD-version), an adaption of the UPPS-P Impulsive Behavior Scale,⁹ a 20-item Likert-rated scale (1=Agree Strongly to 4=Disagree Strongly) that assesses impulsivity. The UPPS-P-CSF used in the current study consists of five subscales: Negative Urgency ($\alpha=.634$), Positive Urgency ($\alpha=.781$), Lack of Planning ($\alpha=.742$), Lack of Perseverance ($\alpha=.695$), and Sensation Seeking ($\alpha=.499$). For externalizing analyses, we examined each of these UPPS-P-CSF subscales. We also examined parent-rated externalizing symptoms using both a KSADS composite of current attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, and conduct disorder symptom summations,^{7,10} as well as the Child Behavior Checklist (CBCL) externalizing measure.¹¹

Other Psychotic-Like Symptom Measures

For a measure of parent-rated child psychotic-like symptoms, within the CBCL,¹¹⁻¹⁷ four questions were identified as measuring psychotic-like symptoms (e.g., "I hear sounds or voices that other people think aren't there," "I see things that other people think aren't there," "I do things that other people think are strange," and "I have thoughts that other people would think are strange."); $\alpha=.879$). Each question was scored from 0=not true, 1=somewhat or sometimes true, and 2=very true or often true.

Neuropsychological Test Battery

Participants completed all tests within the National Institutes of Health Toolbox Cognitive Battery (NIHTB-CB).¹⁸⁻²⁰ The NIHTB-CB consists of 7 tests: Flanker Inhibitory Control and Attention (required participants to focus on a stimulus while inhibiting attention to adjacent stimuli flanking it), List Sorting Working Memory (test of working memory, required participant to sequence different stimuli; e.g., from largest to smallest), Dimensional Change Card Sort (test of cognitive flexibility, required participants to match stimuli on a dimension, wherein the dimension changed periodically without warning), Pattern Comparison Processing Speed (test of processing speed, required participants to discern whether two stimuli were identical or not), Picture Sequence Memory (test of episodic memory, required participants to recall increasingly lengthy series of objects in a particular order), Picture Vocabulary (test of receptive vocabulary, required participants to select the image that most closely matched the meaning of a presented word), and Oral Reading Recognition (required participants read and pronounce letters and words).

Developmental Milestones

The parental assessment battery included questions assessing at what age the child achieved key motor and speech milestones, including rolling over (delayed=6 months or later), sitting (delayed=after 9 months), walking (delayed=after 18 months), and speaking first word (delayed=after 12 months). Questions were scored from 0=achieved within a typical timeframe or 1=delayed. The battery also assessed parental concern regarding motor and speech delays, with parents asked to compare their child's development to that of other children (0=earlier, 1=average, 2=later). Lastly, parent-rated current child clumsiness was assessed¹¹ and scored from 0=not true, 1=somewhat or sometimes true, and 2=very true or often true.

Statistical Analyses

Cronbach's coefficient alpha was used to examine internal consistency of the PQ-BC Total and Distress scores. Distributions of PQ-BC scores were examined for violations of normality assumptions, with these scores

showing substantial positive skewness (with zero values; Total Score skewness: 1.843; Distress score skewness: 3.011). Based on previous recommendations,²¹ scores were logarithmically transformed [formula= $\text{LG10}(X + 1)$], with analyses reported when deviating from non-transformed scores.

Exploratory Factor Analyses (EFAs) were conducted using a promax rotation on a randomly selected half of the data in order to examine the factor structure of Total and Distress scores, based on previous research and factor analysis recommendations.^{22,23} Examination of the scree plots, Horn's Parallel Analysis,²⁴ and Minimum Average Partial,²⁵ were all used to determine the number of factors to retain. Given that the Total score is dichotomous and the Distress score is ordinal, these factor analyses utilized polychoric correlation matrices.

Confirmatory Factor Analyses (CFAs) were conducted (using the lavaan package in R)²⁶ on the other half of the data to examine the fit of the EFA solutions using a weighted least squares, mean and variance (WLSMV) adjusted estimation method, as recommended for non-continuous data.^{27,28} Chi-squared statistics, comparative fit index (CFI), and root mean squared error of approximation (RMSEA) and its 90% confidence interval (CI) and p-value were used to assess model fit from all CFAs. Previous research suggests that $\text{CFI} \geq 0.950$ and $\text{RMSEA} \leq 0.060$ (upper CI bound should be ≤ 0.080) indicate relatively good fit of the tested model compared to the observed data.^{23,29} Although non-significant chi-squared tests indicate good fit, it should be noted that these tests are sensitive to normality assumptions.³⁰

To avoid dependence among participants given that the ABCD sample included twins and siblings, for factor analyses, one individual from each dyad was selected at random for the first dataset, with the other family member selected for a second dataset (family unit was not treated as a clustered variable for factor analyses due to non-convergence of models because of the relatively small number of families with multiple children). While these analyses were run on both datasets, since there with no significant differences compared to the analyses with the entire dataset, only the results from the entire dataset are presented below. Furthermore, for factor analyses, the entire complete questionnaire sample ($n=4523$) was used in order to maximize sample size.

For measurement invariance analyses, since WLSMV requires that participants from each group select each response option for multiple group confirmatory factor analyses, the Distress scores were lumped into three categories: 0, 1 = Distress scores of 1, 2, or 3, and 2 = Distress scores of 4, 5, or 6. The first measurement invariance test was a baseline model testing configural invariance by pooling data across all groups. Invariance in this model suggests that a similar factor structure is present and that the scale items indicate the same latent variable traits (e.g., PLEs) across groups. The second model was a metric (or weak) invariance model, in which item loadings were fixed to be equal across groups. Invariance in this model suggests that the associations between scale items and latent variables are similar across groups. Note that we did not test the metric invariance model for Total Scores, as this model is not appropriate for dichotomous scales.²⁸ The third model was a scalar (strong) invariance model, in which item loadings and thresholds were fixed to be equal across groups. Invariance in this model suggests that the mean response profiles of items are also similar across groups. The last model was a strict invariance model, in which item loadings, thresholds, and unique/residual item variances were fixed to be equal across groups. Invariance in this model indicates that group differences on the scale items are only due to group differences in the latent factors. To examine the fit of each of these four models, the previously mentioned fit statistics (i.e., chi-square, CFI, and RMSEA) were examined, in addition to examining each step-wise change in chi-squared, CFI, and RMSEA from each model to the next, more restrictive model. Previous research indicates that cutoffs of a decrease in $\text{CFI} \leq 0.010$ ³¹ and an increase in $\text{RMSEA} \leq 0.015$ indicate invariance.^{23,32}

Lastly, we performed a model-based mediation analysis using the mediation package in R.³³ This method estimates the presence of mediation as well as the proportion of the link between race and PLEs mediated by income to needs by using a quasi-Bayesian Monte Carlo method with 10,000 simulations.

eTable 2. Original and Modified Versions of Questions and Prevalence of Endorsement

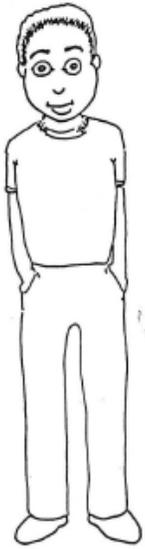
Question Number	Original PQ-B Question	Modified PQ-BC Question	Prevalence PQ-BC Endorsement	Prevalence PQ-BC Endorsement with Distress	Prevalence PQ-BC Endorsement with Significant Distress
1	Do familiar surroundings sometimes seem strange, confusing, threatening or unreal to you?	Did places that you know well, such as your bedroom, or other rooms in your home, your classroom or school yard, suddenly seem weird, strange or confusing to you; like not the real world?	6.0	3.5	1.9
2	Have you heard unusual sounds like banging, clicking, hissing, clapping or ringing in your ears?	Did you hear strange sounds that you never noticed before like banging, clicking, hissing, clapping, or ringing in your ears?	19.8	12.4	4.8
3	Do things that you see appear different from the way they usually do (brighter or duller, larger or smaller, or changed in some other way)?	Did things you looked at seem different than they usually do; like did they seem shinier or darker, larger or smaller or changed in some other way?	11.3	3.4	1.4
4	Have you had experiences with telepathy, psychic forces, or fortune telling?	Did you feel like you had special, unusual powers like you could make things happen by magic, or that you could magically know what was inside another person's mind, or magically know what was going to happen in the future when other people could not?	11.0	1.7	0.8
5	Have you felt that you are not in control of your own ideas or thoughts?	Did you feel that someone else, who is not you, has taken control over the private, personal, thoughts or ideas inside your head?	4.8	3.8	2.2
6	Do you have difficulty getting your point across, because you ramble or go off the track a lot when you talk?	Did you suddenly find it hard to figure out how to say something quickly and easily so that other people would understand what you meant?	18.1	7.3	2.4
7	Do you have strong feelings or beliefs about being unusually gifted or talented in some way?	Did you ever feel very certain that you have very special abilities or magical talents that other people do not have?	11.1	1.1	0.6
8	Do you feel that other people are watching you or talking about you?	Did you suddenly feel that you could not trust other people because they seemed to be watching you or talking about you in an unfriendly way?	19.9	16.0	8.0
9	Do you sometimes get strange feelings on or just beneath your skin, like bugs crawling?	Did your skin or just beneath your skin suddenly start feeling strange, like bugs crawling?	14.5	10.1	4.9

10	Do you sometimes feel suddenly distracted by distant sounds that you are not normally aware of?	Did you lose concentration because you noticed sounds in the distance that you usually don't hear?	14.2	8.5	3.7
11	Have you had the sense that some person or force is around you, although you couldn't see anyone?	Although you could not see anything or anyone, did you suddenly start to feel that an invisible energy, creature, or some person was around you?	20.7	13.3	8.5
12	Do you worry at times that something may be wrong with your mind?	Did you start to worry at times that your mind was trying to trick you or was not working right?	10.3	6.8	4.0
13	Have you ever felt that you don't exist, the world does not exist, or that you are dead?	Did you feel that the world is not real, you are not real, or that you are dead?	6.9	3.4	2.2
14	Have you been confused at times whether something you experienced was real or imaginary?	Did you feel confused because something you experienced didn't seem real or it seemed imaginary to you?	12.0	4.4	1.8
15	Do you hold beliefs that other people would find unusual or bizarre?	Did you honestly believe in things that other people would say are unusual or weird?	12.8	4.3	2.3
16	Do you feel that parts of your body have changed in some way, or that parts of your body are working differently?	Did you feel that parts of your body had suddenly changed or worked differently than before; like your legs had suddenly turned to something else or your nose could suddenly smell things you'd never actually smelled before?	6.7	2.0	0.9
17	Are your thoughts sometimes so strong that you can almost hear them?	Did you feel that sometimes your thoughts were so strong you could almost hear them, as if another person, NOT you, spoke them?	12.7	3.5	1.8
18	Do you find yourself feeling mistrustful or suspicious of other people?	Did you feel that other people might want something bad to happen to you or that you could not trust other people?	13.7	9.3	5.7
19	Have you seen unusual things like flashes, flames, blinding light, or geometric figures?	Did you suddenly start to see unusual things that you never saw before like flashes, flames, blinding light, or shapes floating in front of you?	12.2	6.3	3.4
20	Have you seen things that other people can't see or don't seem to see?	Did you suddenly start to be able to see things that other people could not see or they did not seem to see?	9.9	3.4	2.2
21	Do people sometimes find it hard to understand what you are saying?	Did you suddenly start to notice that people sometimes had a hard time understanding what you were saying, even though they used to understand you well?	14.2	5.5	2.0

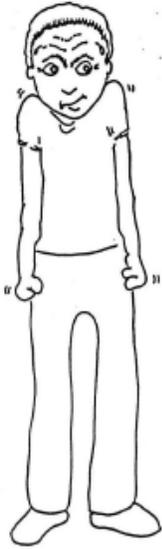
Abbreviations: PQ-B=Prodromal Questionnaire-Brief; PQ-BC=Prodromal Questionnaire-Brief Child version.

eFigure 1.

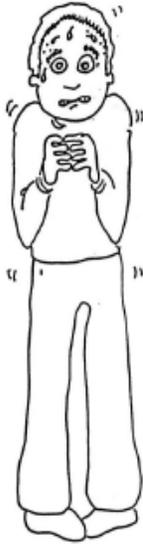
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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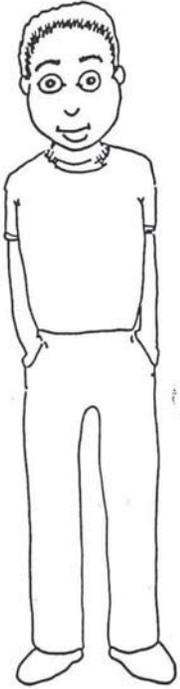
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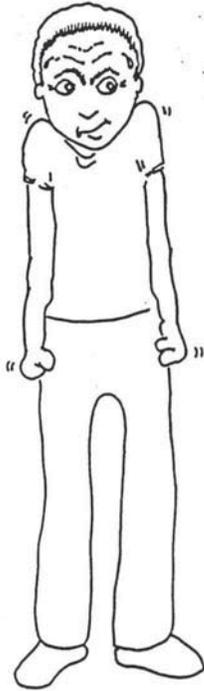
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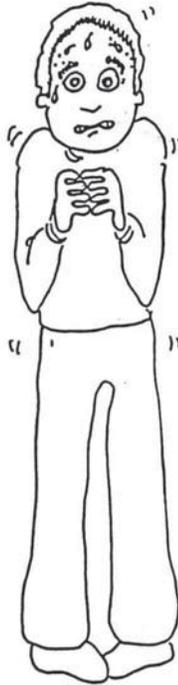
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Did you hear strange sounds that you never noticed before like banging, clicking, hissing, clapping, or ringing in your ears?

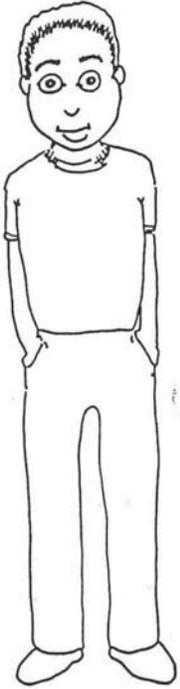
Yes

No

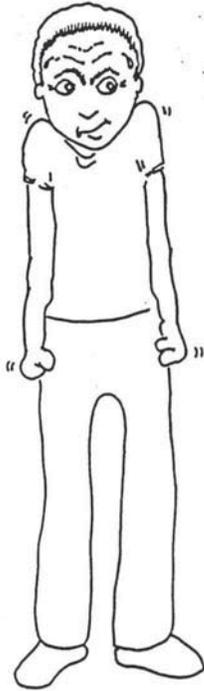
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Did things you looked at seem different than they usually do; like did they seem shinier or darker, larger or smaller or changed in some other way?

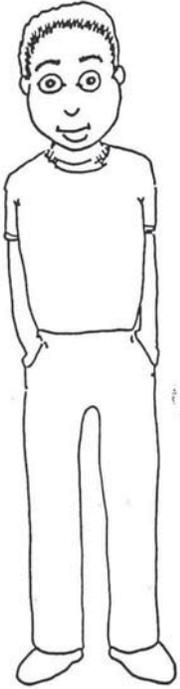
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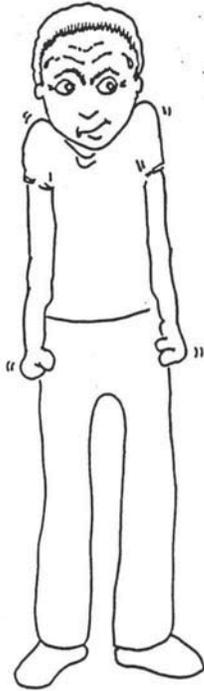
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Did you feel like you had special, unusual powers like you could make things happen by magic, or that you could magically know what was inside another person's mind, or magically know what was going to happen in the future when other people could not?

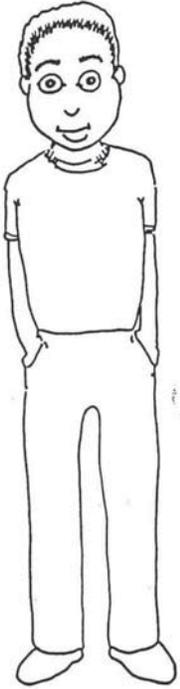
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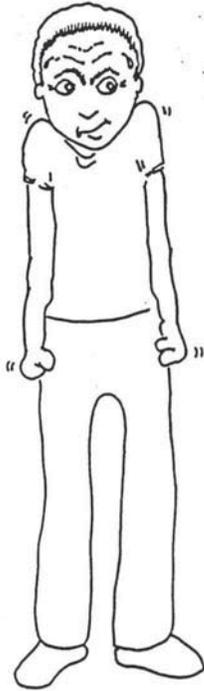
Did it bother you?

Yes No

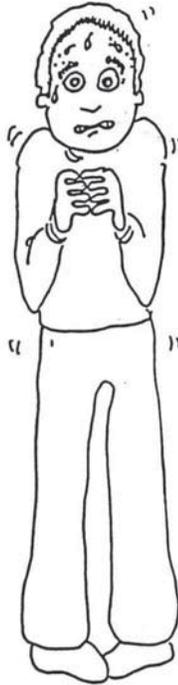
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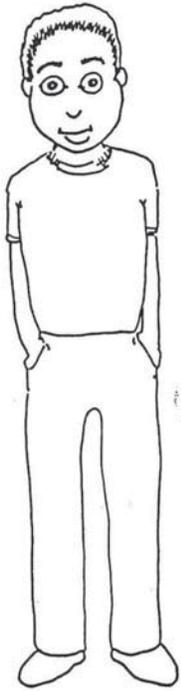
Did you feel that someone else, who is not you, has taken control over the private, personal, thoughts or ideas inside your head?

Yes	No
<input type="radio"/>	<input type="radio"/>

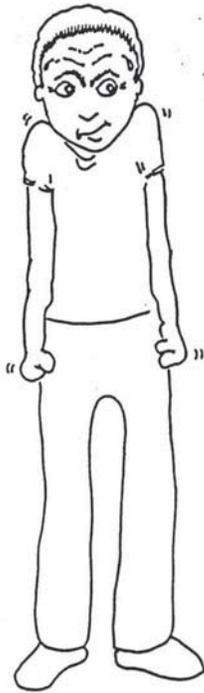
Did it bother you?

Yes No

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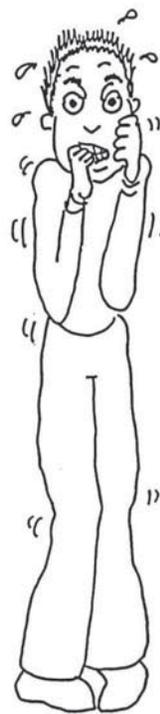
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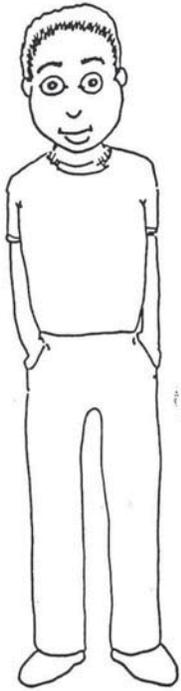
Did you suddenly find it hard to figure out how to say something quickly and easily so that other people would understand what you meant?

Yes	<input type="radio"/>	No	<input type="radio"/>
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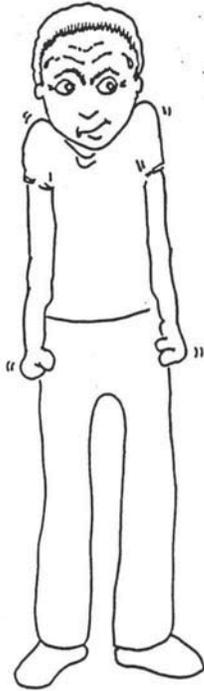
Did it bother you?

<input type="radio"/>	Yes	<input type="radio"/>	No
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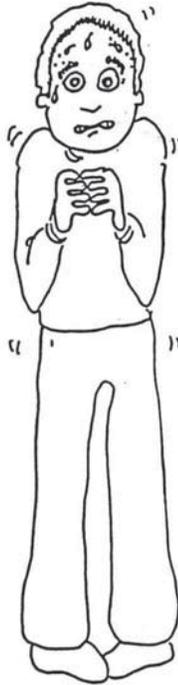
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Which number did you choose?

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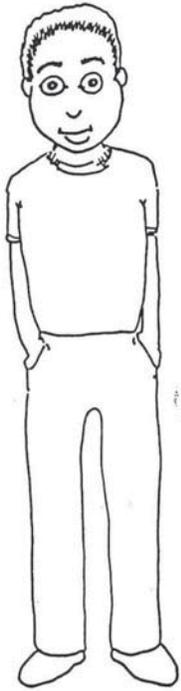
Did you ever feel very certain that you have very special abilities or magical talents that other people do not have?

Yes	No
<input type="radio"/>	<input type="radio"/>

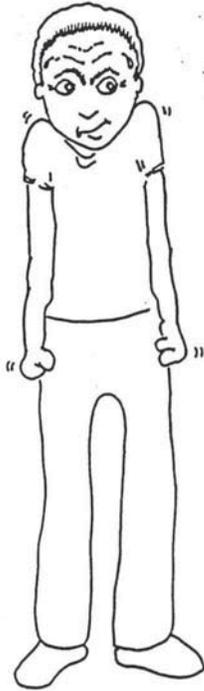
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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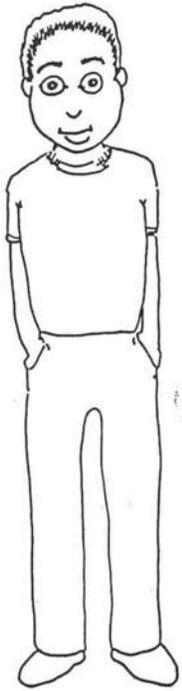
Did you suddenly feel that you could not trust other people because they seemed to be watching you or talking about you in an unfriendly way?

Yes	No
<input type="radio"/>	<input type="radio"/>

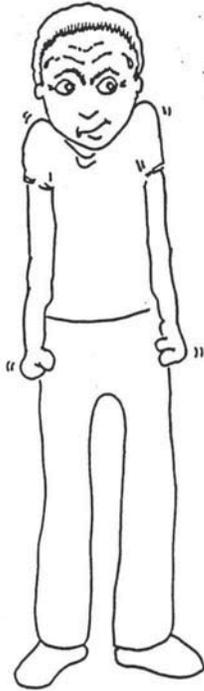
Did it bother you?

Yes No

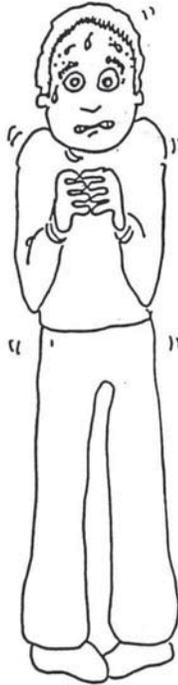
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Did your skin or just beneath your skin suddenly start feeling strange, like bugs crawling?

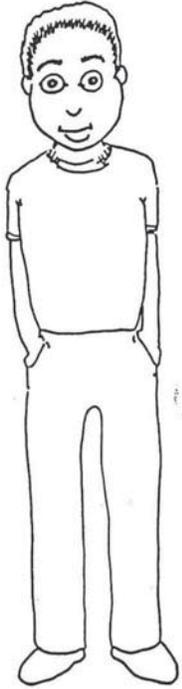
Yes

No

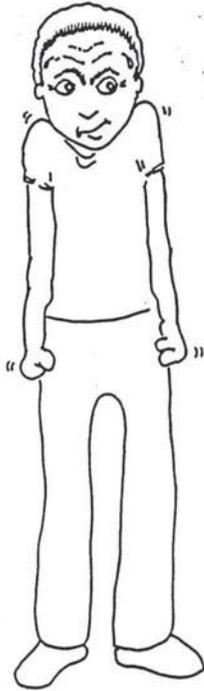
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you lose concentration because you noticed sounds in the distance that you usually don't hear?

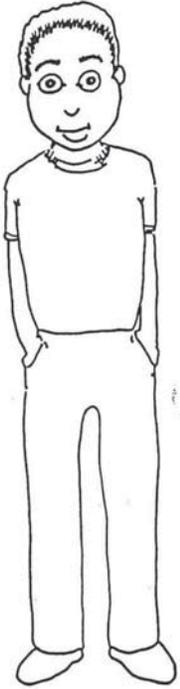
Yes

No

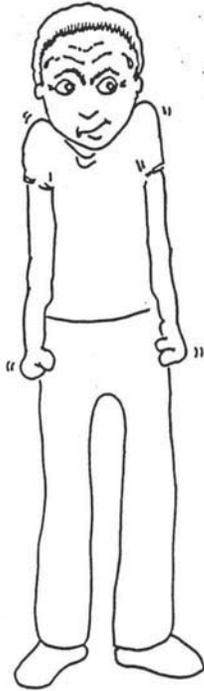
Did it bother you?

Yes No

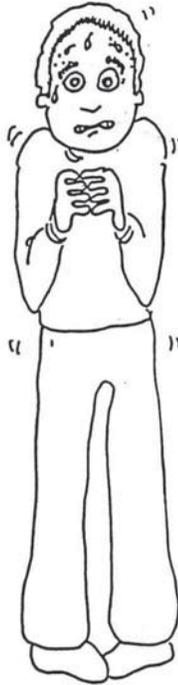
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Although you could not see anything or anyone, did you suddenly start to feel that an invisible energy, creature, or some person was around you?

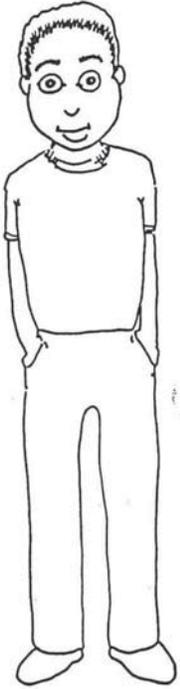
Yes

No

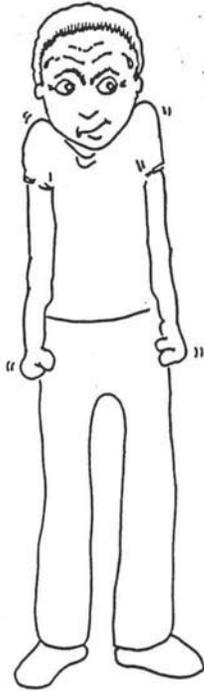
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

	1	2	3	4	5
	<input type="radio"/>				

Did you start to worry at times that your mind was trying to trick you or was not working right?

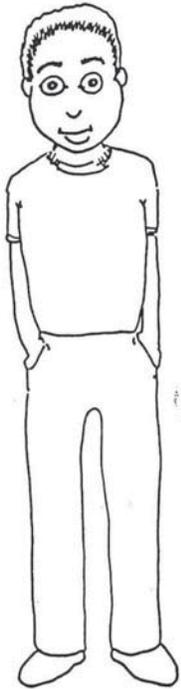
Yes	No
<input type="radio"/>	<input type="radio"/>

 Describe the event.
 What do you mean?
 What was it that happened?
 Did you think that maybe it wasn't real?

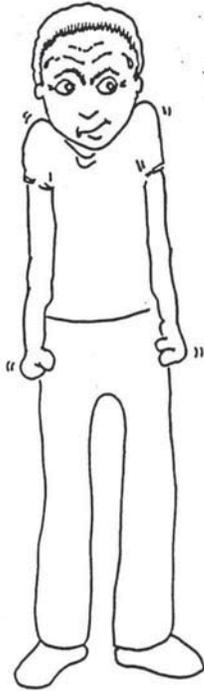
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you feel that the world is not real, you are not real, or that you are dead?

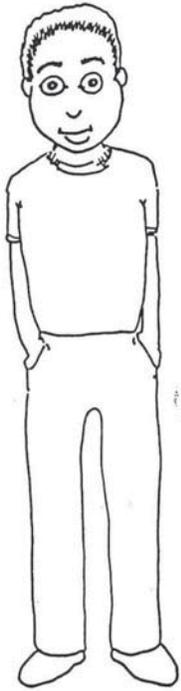
Yes

No

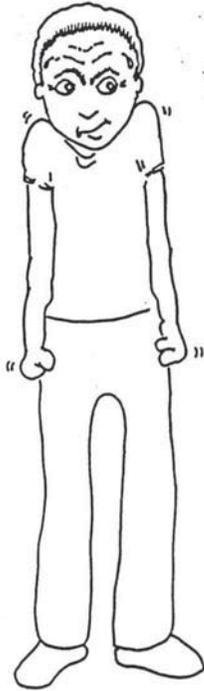
Did it bother you?

Yes No

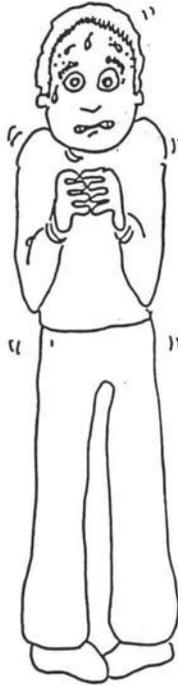
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you feel confused because something you experienced didn't seem real or it seemed imaginary to you?

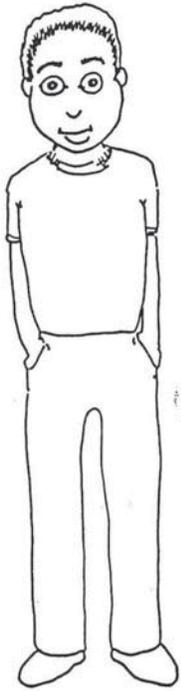
Yes

No

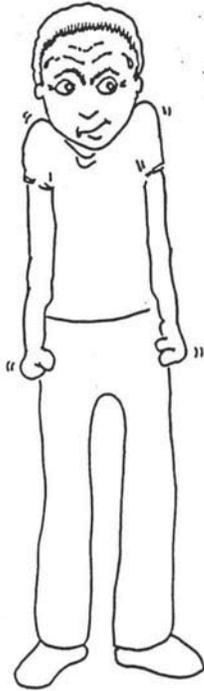
Did it bother you?

Yes No

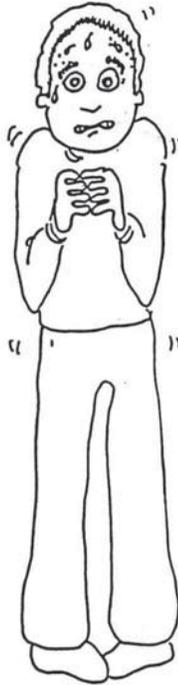
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you feel that parts of your body had suddenly changed or worked differently than before; like your legs had suddenly turned to something else or your nose could suddenly smell things you'd never actually smelled before?

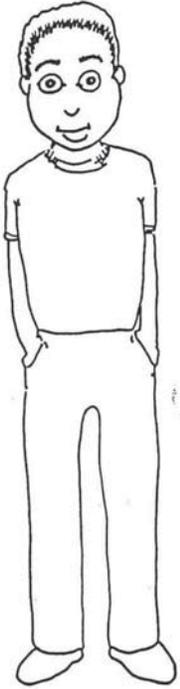
Yes

No

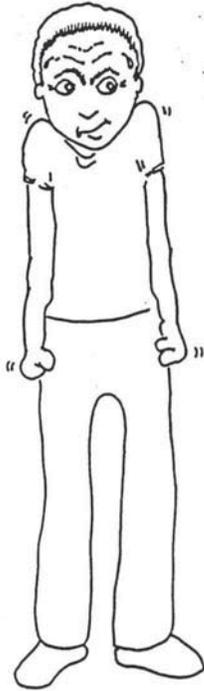
Did it bother you?

Yes No

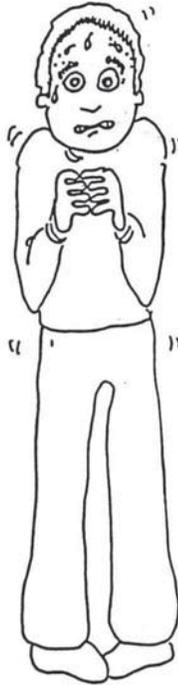
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



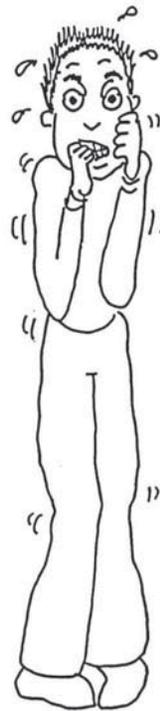
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Which number did you choose?

1	2	3	4	5
<input type="radio"/>				

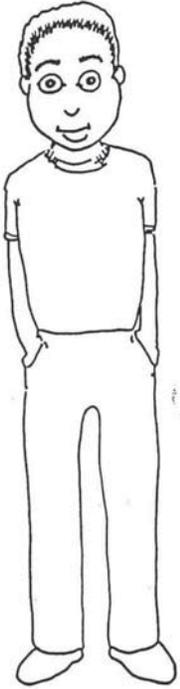
Did you feel that sometimes your thoughts were so strong you could almost hear them, as if another person, NOT you, spoke them?

Yes	No
<input type="radio"/>	<input type="radio"/>

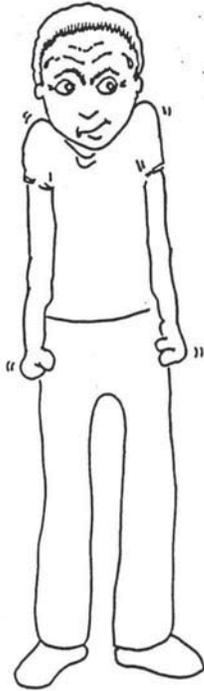
Did it bother you?

Yes No

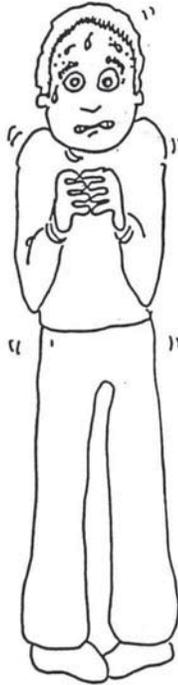
Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you feel that other people might want something bad to happen to you or that you could not trust other people?

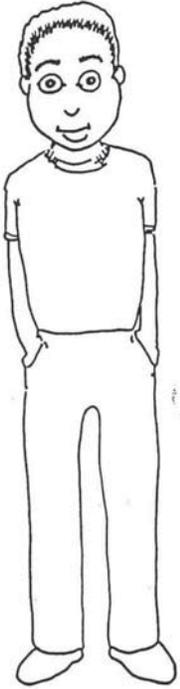
Yes

No

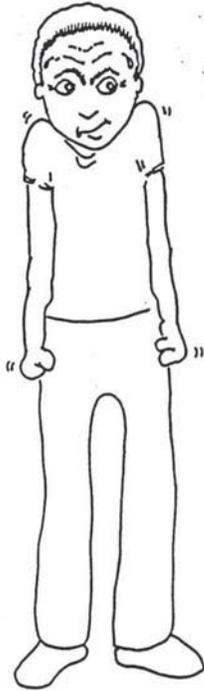
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you suddenly start to see unusual things that you never saw before like flashes, flames, blinding light, or shapes floating in front of you?

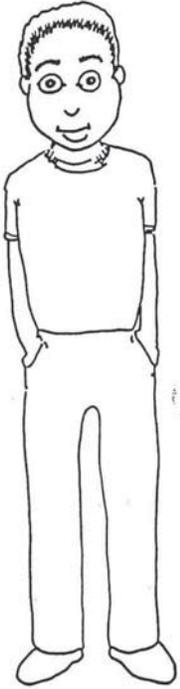
Yes

No

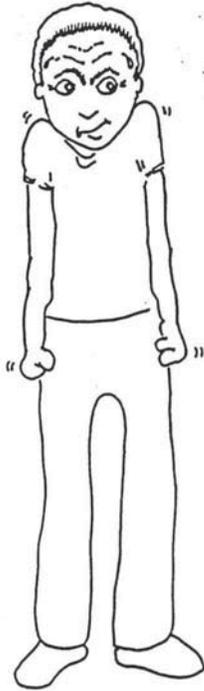
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

1	2	3	4	5
<input type="radio"/>				

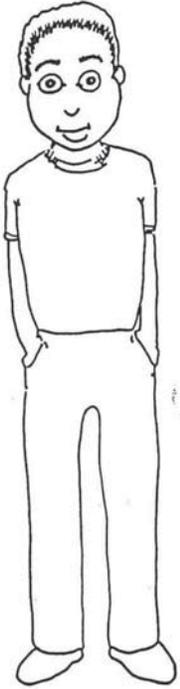
Did you suddenly start to be able to see things that other people could not see or they did not seem to see?

Yes	No
<input type="radio"/>	<input type="radio"/>

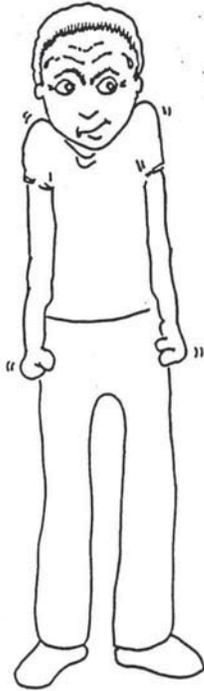
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?

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Did you suddenly start to notice that people sometimes had a hard time understanding what you were saying, even though they used to understand you well?

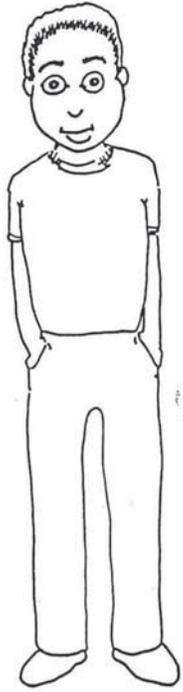
Yes

No

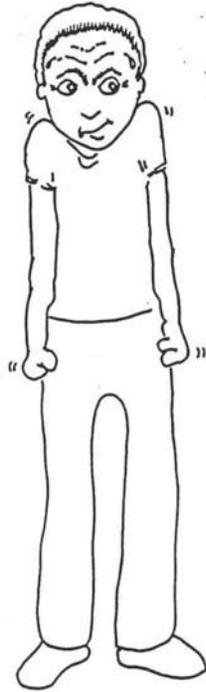
Did it bother you?

Yes No

Please CHOOSE THE NUMBER below the appropriate picture that shows us how much that bothered you when it happened.



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Which number did you choose?