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Choice Reaction Time Increases with Age during the Preclinical Phase in Presenilin-1 Mutation Carriers

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OBJECTIVE: To determine the effect of a Presenilin-1 (PS1) mutation on simple and choice reaction time (RT) in pre-clinical autosomal dominant Alzheimer's disease (AD).

BACKGROUND: Previous studies have suggested that decline in delayed verbal memory is the earliest change to occur in incipient AD. These neuropsychological testing procedures may, however, be insensitive to decrements in speed of information processing that could precede this memory decline. Studies employing RT protocols have shown that slowing in simple RT is an accompaniment of normal aging but may also herald the onset of dementia. Other studies suggest that RT in tasks requiring more complex cognitive processing is more specific for incipient dementia.

DESIGN/METHODS: We employed computerized testing to measure RT in simple and choice paradigms in Mexican persons at-risk for inheriting a PS1 mutation. Subjects were children of patients with clinically probable AD associated with the A431E mutation in the PS1 gene. Subjects were not excluded if subjective memory complaints or cognitive decline had been noted but were excluded if they had experienced functional decline. Subjects underwent 3 hours of neuropsychological testing and 1/2–1 hour of computer-based RT testing. Seven tests were administered on a lap-top computer including a test in which the subject makes a key press when a cross-hair appears on the screen (simple RT). In the choice RT paradigm subjects decided whether a Spanish noun and pictured object corresponded or not. In a subset of signalled trials subjects had to reverse their response. Subjects practiced until a baseline level of performance was obtained before responses were recorded.

RESULTS: A total of 25 subjects were tested of which 16 (representing 4 distinct families) underwent genetic testing. Of these, 7 (2 male, 5 female) carried the A431E mutation and 9 at-risk relatives (1 male, 8 female) did not. Mini-Mental State Examination scores did not differ between the groups (28 for mutation carriers and 28.3 for non-carriers, p=.726). Ages ranged from 19 to 49. In the simple RT task, there was no significant correlation between age and RT in either the mutation carriers (Pearson's r.095, p=.839) or the non-mutation carriers (r.087, p=.824). In the choice RT task however, a significant positive correlation between age and RT was found in the mutation carriers (r=.867, p=.012) but not in the non-mutation carriers (r=.379, p=.315). Mean error rate was non-significantly higher for the mutation carriers than for the non-carriers.

CONCLUSIONS: This study suggests that cognitive processing time as measured in a choice RT task occurs prior to changes in simple RT in at-risk subjects carrying a PS1 mutation. This task, which requires inhibition of a learned response, may be particularly sensitive to early cognitive decline in AD. Further studies with more subjects are necessary to determine the relationship of this change to other neuropsychological and functional indices.

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