Measuring cognitive change in subjects with prodromal Alzheimer's disease

T Mura*, MD, PhD [1, 2, 3, 4], C Proust-Lima, PhD [5, 6], H Jacqmin-Gadda PhD [5, 6], TN Akbaraly PhD [1,2,7], J. Touchon, MD, PhD[8 ,2], B Dubois, MD, PhD [9], C Berr, MD, PhD [1, 2, 8].

[1] INSERM, U1061, Neuropsychiatrie : Recherche Epidémiologique et Clinique, 34093 Montpellier, Cedex 5, France

[2] Université Montpellier I, 34095 Montpellier, Cedex 5, France

[3] Département d'Information Médicale & Centre d'Investigation Clinique, CHRU Montpellier, 34093 Montpellier, France

[4] INSERM, CIC 1001, Montpellier, France

[5] INSERM U897, Equipe de Biostatistique, Centre de Recherche en Epidémiologie et Biostatistique, F-33076 Bordeaux, France

[6] Université Bordeaux Segalen, ISPED, F-33076 Bordeaux, France

[7] Department of Epidemiology and Public Health, University College London, London, United Kingdom.

[8] CMRR Languedoc Roussillon, service de Neurologie, CHRU Montpellier, 34093Montpellier, France

[9] INSERM-UPMC UMRS 975, Institut de la Mémoire et de la Maladie d'Alzheimer, ICM, APHP, Salpétrière Hospital, University Paris 6, Paris, France

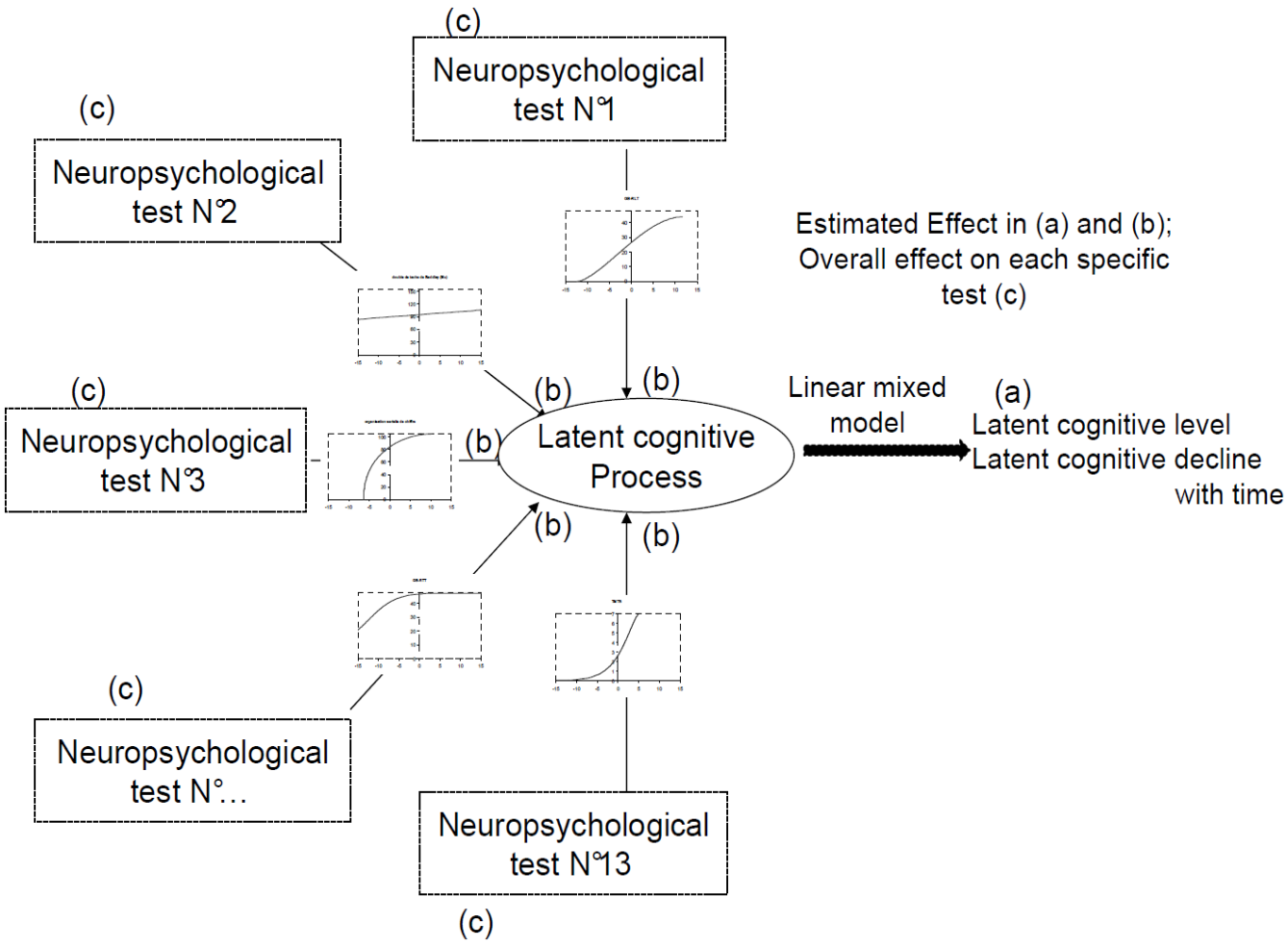
Corresponding author: Thibault Mura

INSERM U1061, Hôpital La Colombière, 39 Avenue Charles Flahault, BP 34493, 34093 Montpellier, Cedex 5, France.

Phone: 33 (0)4 67 33 23 28, Fax: 33 (0)4 67 33 23 35

email: t-mura@chu-montpellier.fr

Figure 1: Conceptualization of the nonlinear mixed model involving a latent process to model cognition from several neuropsychological tests.

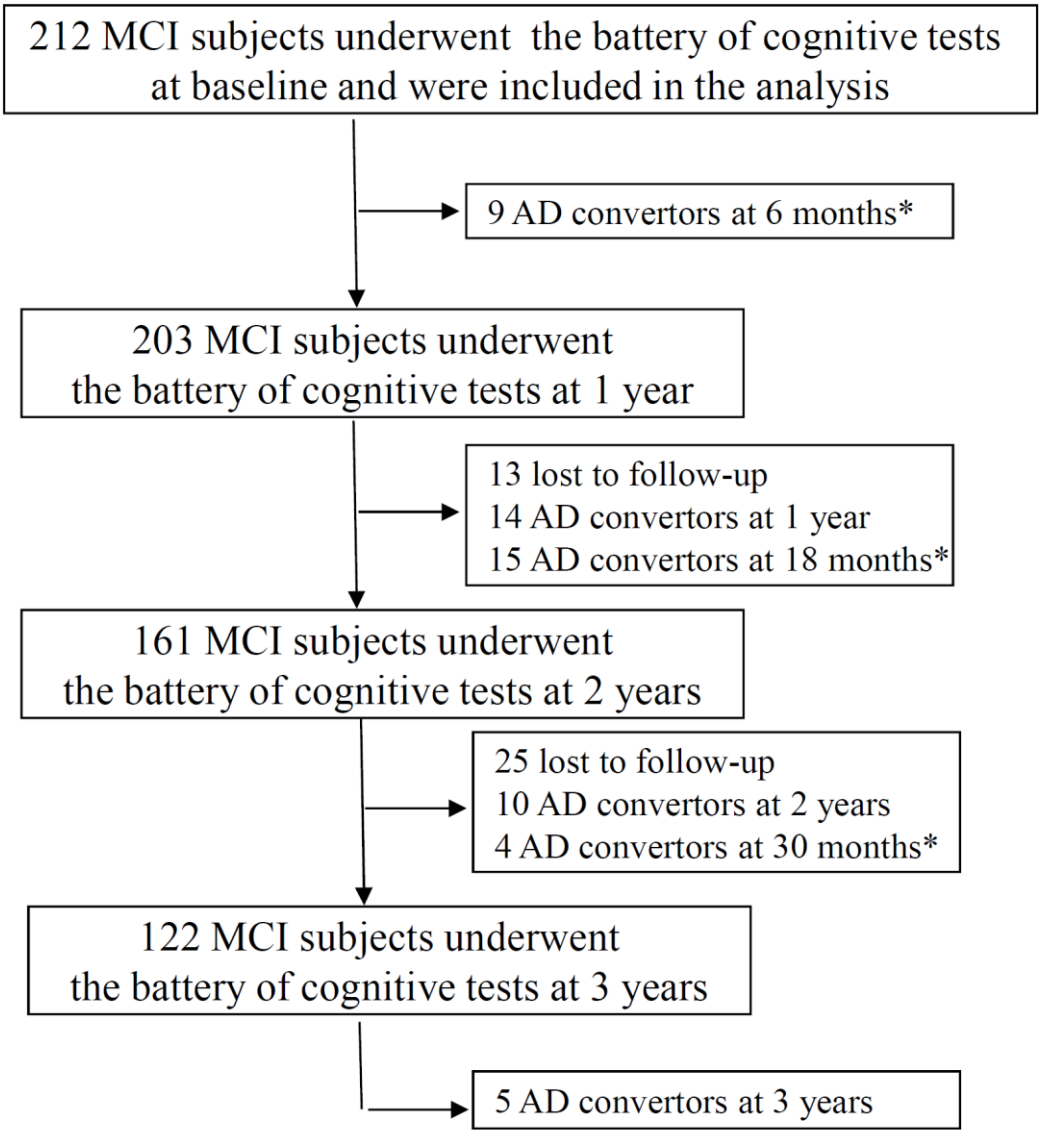


(a) A linear mixed model describes the change over time in the latent cognitive process and evaluates the common effects of covariates on this latent cognitive trajectory

(b) Test-specific measurement models relate each administration of the psychometric tests with the latent cognitive process, by accounting for and describing the metrological properties of the tests and test-specific associations with covariates.

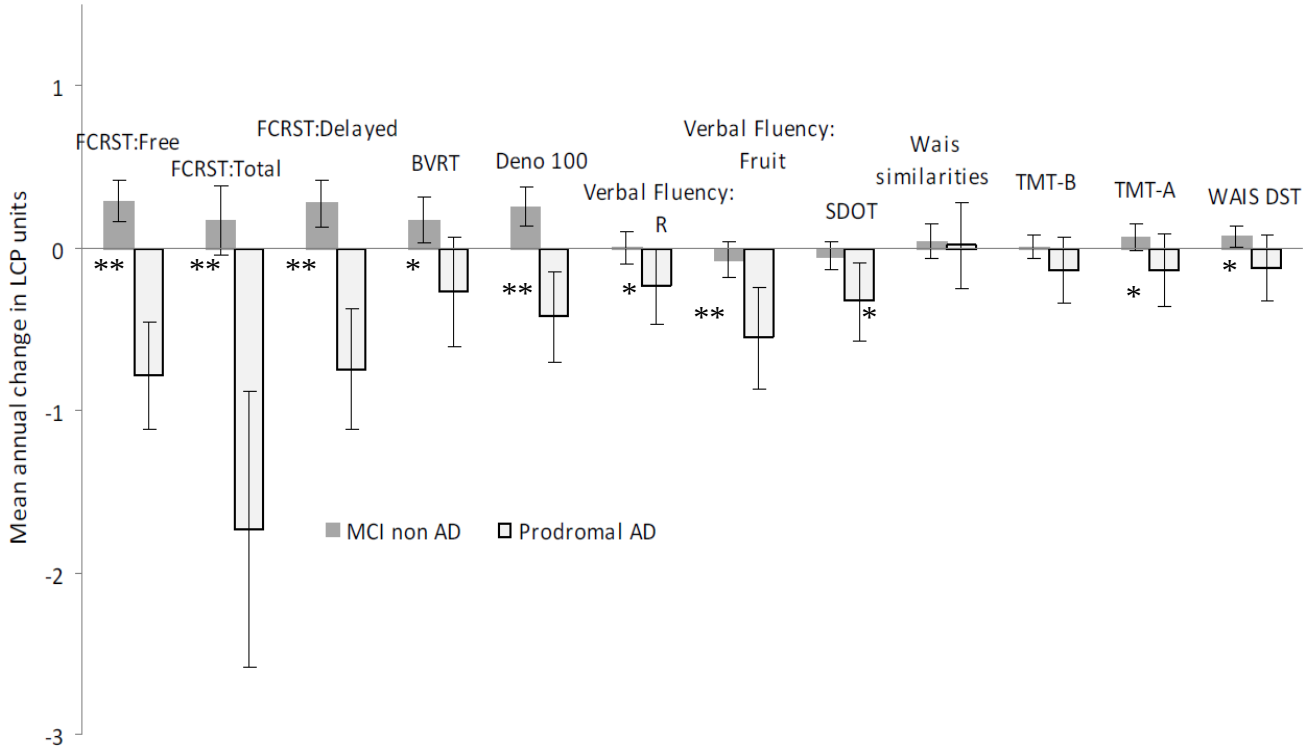
(c) Overall effect of a covariate on each specific test is calculated by adding together the effect of the covariate on the latent cognitive process (a) and the test-specific effect (b).

Figure 2: Diagram mapping the administration of the neuropsychological tests and the occurrence of AD during the three-year follow-up (FU) of the study.



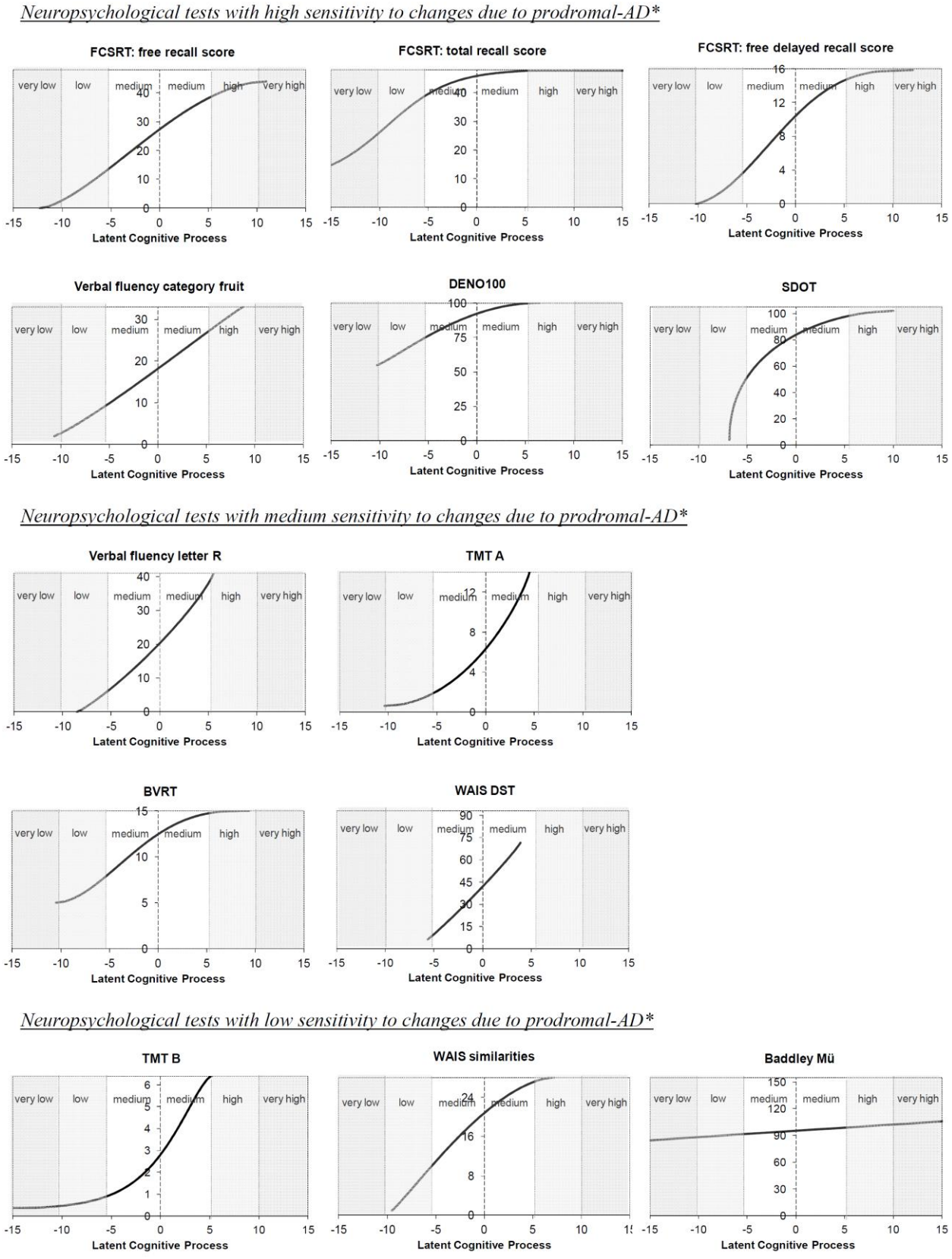
* In the event of a suspected conversion, the patient underwent an additional neuropsychological evaluation 6 months later.

Figure 3: Mean annual change for each neuropsychological test according to the occurrence of AD during the follow-up (in latent cognitive process units).



Mean annual change with 95% confidence interval for each neuropsychological test (in latent cognitive process unit) for a 71.8 year-old woman with a low level of education.
*denotes a significant difference (adjusted for age, sex and level of education) between Prodromal-AD and MCI Non-AD ($p<0.05$), ** for $p<0.01$
Baddeley Mü was not represented in this figure because of its high level of individual variability; this test did not significantly change over time in any group and was not different between groups.

Figure 4: Metrological properties of the thirteen neuropsychological scores used in the study



*according to the previous results display in figure 3