Altered Effect of Dopamine Transporter 3’UTR VNTR Genotype on Prefrontal and Striatal Function in Schizophrenia

Diana P. Prata, PhD; Andrea Mechelli, PhD; Marco M. Picchioni, MD; Cynthia H. Y. Fu, MD, PhD; Timothea Toulopoulou, PhD; Elvira Bramon, MD, PhD; Muriel Walshe, PhD; Robin M. Murray, MD, PhD; David A. Collier, PhD; Philip McGuire, MD, PhD

Arch Gen Psychiatry. 2009;66(11):1162-1172

eMETHODS

Verbal Fluency Task

Under the experimental condition, subjects were instructed to overtly generate a word in response to a visually presented letter. Each condition was presented in blocks lasting 28 seconds, with 7 presentations of a given letter per block and an interstimulus interval (ISI) of 4 seconds. The experimental condition alternated with the control condition and with repetition of the word rest, and 5 blocks of each condition were performed. An ISI of 4 seconds was selected on the basis of the pilot study. As the response time for the letters used ranged from 1.2 to 2.3 seconds, the “silent” period between the acquisition of clustered image volumes was set at 2.9 seconds. Coupled with an image volume acquisition of 1.1 seconds (see the next section), the resultant ISI was 4 seconds. The “easy” condition was 1 of 2 sets of letters: T, L, B, R, S or T, C, B, P, S; and the “hard” condition was either O, A, N, E, G or I, F, N, E, G because this number of stimuli has provided sufficient power to detect regional activation. The order of the easy and hard runs was counterbalanced across subjects. Subjects were presented with 1 set of easy and hard letters in separate blocked runs (5 blocks for each experimental condition) with the order of presentation randomized between subjects. Verbal responses were recorded via a magnetic resonance imaging–compatible microphone on audio software (Cool Edit 2000; Syntrillium Software Corp [now owned by Adobe Systems, San Jose, California]). Incorrect responses were defined as words that were proper names, repetitions, or grammatical variations of the previous word and “pass” responses.

Image Acquisition

Seventy-four T2*-weighted volume images were acquired for each condition on a 1.5-T imager retrofitted with echo planar imaging capability (GE Signa System; General Electric, Milwaukee, Wisconsin) at the Maudsley Hospital, South London National Health Service Trust, England. Twelve noncontiguous axial planes (7-mm thickness; section skip, 1 mm) parallel to the anterior commissure–posterior commissure line were collected during 1100 milliseconds in a clustered acquisition (echo time, 40 milliseconds; 70° flip angle). With a repetition time of 4000 milliseconds, there remained a relatively silent period of 2900 milliseconds for each stimulus. During this period, a letter was presented (with a height of 7 cm and subtending a 0.4° field of view) immediately after each acquisition within a rectangular outline for 750 milliseconds, after which the outline remained and a single overt verbal response could be made. Head movement was minimized by a forehead strap, and subjects wore noise insulated ear protectors. To ensure that subjects heard their responses clearly and to more closely mimic usual speaking conditions, their speech was amplified by a computer sound card and then relayed to the subject through an acoustic magnetic resonance imaging sound system (Ward Ray, Hampton Court, England) and pneumatic tubes within the ear protectors at a volume of 91 (±2) dB.