Archival Report

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Impaired Communication Between the Motor and Somatosensory Homunculus Is Associated With Poor Manual Dexterity in Autism Spectrum Disorder

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ABSTRACT

BACKGROUND: Fine motor skill impairments are common in autism spectrum disorder (ASD), significantly affecting quality of life. Sensory inputs reaching the primary motor cortex (M1) from the somatosensory cortex (S1) are likely involved in fine motor skill and specifically motor learning. However, the role of these connections has not been directly investigated in humans. This study aimed to investigate, for the first time, the role of the S1-M1 connections in healthy subjects in vivo and whether microstructural alterations are associated with motor impairment in ASD.

METHODS: Sixty right-handed neurotypical adult men aged 18 to 45 years, and 60 right-handed age- and sex-matched subjects diagnosed with ASD underwent fine motor skill assessment and scanning with diffusion tensor imaging (DTI). The streamlines of the hand region connecting S1-M1 of the motor-sensory homunculus were virtually dissected using TrackVis, and diffusion properties were extracted. The face/tongue region connections were used as control tracts.

RESULTS: The ASD group displayed lower motor performances and altered DTI measurements of the hand-region connection. Behavioral performance correlated with hand-region DTI measures in both groups, but not with the face/tongue connections, indicating anatomical specificity. There was a left-hemisphere association of motor ability in the control group and an atypical rightward shift in the ASD group.

CONCLUSIONS: These findings suggest that direct interaction between S1 and M1 may contribute to the human ability to precisely interact with and manipulate the environment. Because electrophysiological evidence indicates that these connections may underpin long-term potentiation in M1, our findings may lead to novel therapeutic treatments for motor skill disorders.

Keywords: Autism, Diffusion tensor imaging, Homunculus, Motor skill, Primary motor cortex, Somatosensory cortex, Tractography

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The development of fine motor skills for precision grasping has been crucial to achieving greater control of the environment throughout evolution. This is particularly true for humans who have acquired the finest ability to manipulate objects for a wide range of activities that are characteristic of our species, from tool making to writing and artistic expression. Skillful hand motor ability depends on precise movement of the thumb and forefingers, which is under the direct control of the primary motor cortex (M1) (1).

The neurons of M1 are arranged according to a topographical map of the opposite body half. A distinct feature of this map consists of the disproportionate representation of neurons controlling those muscles capable of finely controlled movements, generally referred to as the motor homunculus (2). For instance, the largest areas in M1 are occupied by neurons controlling finger movements, followed by neurons for lips and tongue movement. A similar topographical organization has been described for the primary somatosensory cortex (S1) in the parietal lobe (i.e., the somatosensory homunculus). Here, areas dedicated to the representation of tactile and proprioceptive information from the fingers and oral region are larger than other body parts.

We have recently demonstrated in humans that the motor and somatosensory homunculi are directly connected through short U-shaped fibers running beneath the central sulcus (3). The pattern of distribution of these fibers follows the topographical organization of M1 and S1. That is, greater connections exist between finger regions compared with areas controlling other body parts. The existence of these connections in humans is consistent with previous reports supporting

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the role of somatosensory inputs in motor learning and precision grasping in animals (4–6). In monkeys, inactivation of S1 leads to altered finger coordination, such as the inability to oppose the thumb and forefinger and the inaccurate control of grip forces (4,7). Furthermore, experimental studies in healthy humans have demonstrated that in conditions of digital anesthesia, where tactile sensation is absent, coordination of thumb and finger movements is impaired due to misalignment of fingers and an imbalance of the pressure applied (8). These studies suggest that direct connections between S1 and M1 may play a crucial role in precision grasping movements, although direct experimental evidence for this is lacking in humans (9,10).

In the present study we therefore sought evidence of the role of S1-M1 connections in fine motor skill and precision grasping ability. To investigate this, first we combined behavioral measurements of fine motor skill performance with diffusion tensor tractography in a group of 60 healthy adults to understand the association between grasping performance and microstructural properties of U-shaped fibers connecting S1 to M1 of the hand region. As a control tract we also investigated the U-shaped connections of the face/tongue region, the microstructure of which would not be predicted to correlate with finger dexterity.

Second, we obtained diffusion tractography and grasping performance in a group of adults with a neurodevelopmental disorder in which precision grasping abnormalities are prevalent, namely autism spectrum disorder (ASD). ASD affects approximately 1% of the population and is diagnosed on the basis of social-communication impairments, alongside repetitive and stereotypic behaviors (11). Motor abnormalities have been reported in up to 79% of people with ASD (12). These abnormalities include precision grasping impairments (13). Motor impairments are present across the spectrum of autism (14) and are reported to be some of the earliest signs of ASD to emerge in infancy (15). Motor difficulties can significantly reduce day-to-day quality of life because of altered peer group interactions through sport and other social activities and increased dependence on others (16). Furthermore, motor proficiency is a necessary prerequisite for interaction with the environment, which underpins the development of social and language skills (17), highlighting the importance of investigating motor deficits in ASD. ASD is also associated with the abnormal development of white matter connections. A large number of studies have found that children and adults with ASD display structural differences in white matter tracts and across multiple brain regions (18). We therefore investigated whether abnormal structure of the S1-M1 U-shaped fibers underpins precision grasping difficulties in 60 right-handed adult men with ASD.

METHODS AND MATERIALS

Participants

Sixty neurotypical adult men aged 18 to 45 years, and 60 age- and sex-matched subjects with a diagnosis of ASD were recruited at the Institute of Psychiatry, Psychology and Neuroscience, King's College London, or the Autism Research Centre, University of Cambridge, as part of the UK Medical Research Council Autism Imaging Multicentre Study. Approximately equal ratios of cases to controls were recruited at each site: Institute of Psychiatry, Psychology and Neuroscience, 34:32, University of Cambridge, 26:28. All participants were right-handed, as indicated by a score of +40 or higher on the Edinburgh Handedness Inventory (19).

Exclusion criteria for all subjects included any medical illness affecting brain function or history of epilepsy, intellectual disability, major psychiatric disorder such as psychosis and attention-deficit/hyperactivity disorder (ADHD), head injury, or genetic disorder associated with autism. Participants taking any current psychotropic medications, including antipsychotic medication, mood stabilizers, benzodiazepines, stimulants, and selective serotonin reuptake inhibitors, or with a history of substance abuse were excluded. ASD participants met the ICD-10 research criteria. This was confirmed with the Autism Diagnostic Interview-Revised (20). All cases with ASD met Autism Diagnostic Interview-Revised algorithm cutoff values in the three domains of impaired reciprocal social interaction, communication, and repetitive behaviors; however, one point below cutoff in one of the domains was permitted (Table 1).

Current symptoms were assessed using the Autism Diagnostic Observation Schedule (21) but not as inclusion criteria. All participants underwent a neuropsychological test battery (22). This included the Wechsler Abbreviated Scale of Intelligence (23) as a measure of overall intellectual ability. All participants fell within the high-functioning range on the autism spectrum as defined by a full-scale IQ of >70. Written consent was acquired for all participants after a complete description of the study was given, in accordance with ethics approval by the National Research Ethics Committee, Suffolk, England.

Table 1. Subject Demographic Characteristics

Characteristic	Healthy Controls (n = 60)	Subjects With Autism (n = 60)
Age, Years[a]	29 (7) [18–45]	26 (7) [18–43]
WASI IQ Score[a]		
Full scale	111 (12) [88–133]	115 (12) [77–137]
Verbal	108 (13) [84–139]	112 (13) [71–137]
Performance	111 (13) [88–133]	115 (13) [75–137]
ADI-R Score		
Total	NA	39 (10) [21–62]
Social	NA	18 (5) [9–28]
Communication	NA	14 (4) [8–24]
Repetitive	NA	5 (2) [2–10]
ADOS Score[b]		
Total	NA	11 (5) [1–23]
Social	NA	6 (3) [1–14]
Communication	NA	3 (2) [0–7]
Repetitive	NA	1 (1) [0–6]

Data are mean (SD) [range].

ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; NA, not applicable; WASI, Wechsler Abbreviated Scale of Intelligence.

[a]No significant between-group differences were found in age, full-scale IQ, verbal IQ, or performance IQ (all $p > .05$, 2-tailed).

[b]Information was available for 58 subjects with autism.