PARKINSON'S DISEASE: MUCH MORE THAN A NEURO-MOTOR DISABILITY. STUDY ON MOTOR-COGNITIVE AND PERCEPTION RELATED ASPECTS IN PATIENTS IN WORKING AGE THROUGH A VALUABLE TOOL: HANDFORCE

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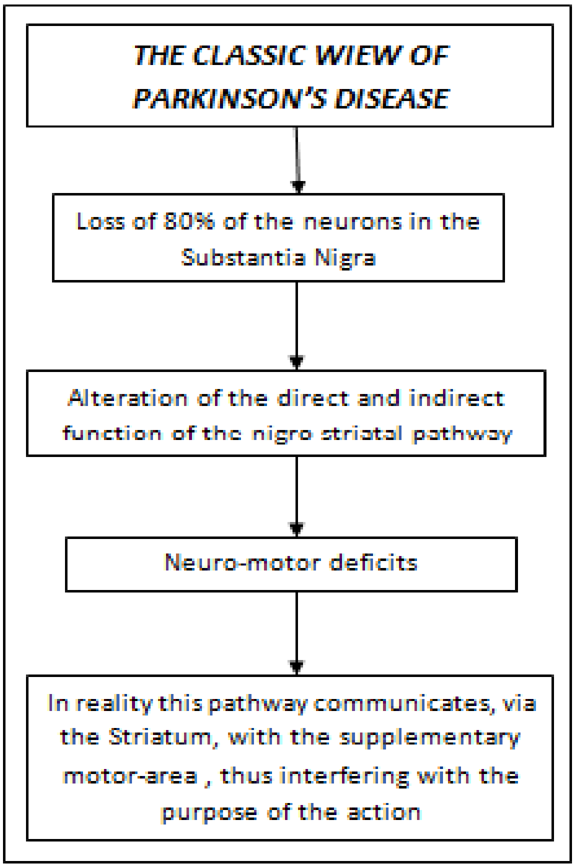
Hand-motion control is one of the most complex concepts in modern neurology, which cannot neglect neurocognitive, neuromotor, exteroceptive and proprioceptive aspects or the elaboration of this information. The hand is the exploration- and fact-finding tool par excellence; it is through the hand that the child will explore the world and it is through the hand that we know the world and act on it.

In patients with the PD, the neuro-cognitive aspect reveals itself through the disexecution Syndrom, which takes the form of apraxia in the hand. The motor-deficit expresses itself as akynesia, stiffness and bradikynesia, while the proprioceptive and exteroceptive deficits are expressed as peripheral and central ataxia.



Introduction

In addition to the nigrostitial pathway, there are at least three additional, physiological, dopaminergic pathways with a different origin and with projections and functions which are completely different from purely neuro-motor ones. Despite they respectively depart as follows: (1) (11) (21)

a) Mesolimbic pathway from the frontal tegmental area;

b) The mesocortical pathway from the ventral tegmental area;

c) The tubero- infundibular pathway from the tuberal area in the arcuate nucleus in the mediobasal hypothalamus

They too consist of dopaminergic neurons, which are genetically similar although differently located.With the Parkinson disease, therefore, you experience a loss of neurons also along the above-mentioned pathways, which is nevertheless less obvious because of their more sparse distribution than in the Substantia Nigra, where their concentration is higher.

The neurocognitive impairment

The mesolimbic pathway reaches from the ventral tegmental area to the Nucleus Accumbens in the limbic system, through the Amygdala and Hippocampus down to the medial, pre-frontal cortex (25) (36). This pathway is on one hand responsible for managing the functioning of the

Nucleus Accumbens , (27) (28) that is tightly related to reward, on of the other.hand is responsible of the amygdala which is related to episodic, autobiographic memory , to emotional memory and reward, to attention and specifically to someone's ability to pay attention to a specific stimulus and also to the ability to assess someone's reliability just based on appearance (first sight-impression). This pathway (34) (35) also projects to the Hippocampus is related to *long-term memory, spatial memory* the *what, when, where* memory and the ability to learn through a task. The mesocortical pathway goes from the ventral tegmentum to the frontal and pre-frontal cerebral cortex . It manages the *cognitive motor planning* that is the organization and recruiting of complex movements aimed at completing a task and the integration of sensory and mnemonic information. All the deficits due to impaired cognitive functioning in the pre-frontal and frontal area, (36) (38) (39) (40) together with problems related to limbic derangements and the frontal striate projections give origin to dis-executional syndromes in the hand that will manifest themselves as ideational apraxia and motor apraxia. Ideational apraxia (55) (56) (57) is a voluntary movement-disorder, where the patient has difficulties identifying the purpose of an object. The dysfunction is all about the mental representation of the gesture or the movement sequence: they do not know the meaning of the object and are not able to make or remember plans to achieve their objectives. Whenever they manage to plan a motion sequence, it might be incomplete or wrong. Motion ability is not lost: the areas designed for ideation and planning are damaged. The patient's movements are confused: during object-usage tests, frequent omissions, mistaken usage, wrong localization, a clumsy behavior, doubtfulness and sequence errors are noted (e.g.: when trying to light up a cigarette with a match, the patient will keep the match in their hand until it burns their fingers). Ideo-motor apraxia (IMA) is the situation whereby the subject is no longer able to translate an idea into a movement. The patient can recognize the object and its function, he/she knows how to use it, but is unable to execute the task upon request (e.g. the patient can correctly use scissors, but cannot do this upon request) . The link between the prefrontal area, where ideation takes place, and the area designed for motion planning in the motor cortex is interrupted.

The ataxia

As regards the peripheral component, literature reports (58) (59) (60) deep and superficial sensitivity deficits. At superficial level , tactile, thermal and pain- hypoesthesia is noticeable (in the epicritical and protopatic components). For example, during a complex action, like lightening a cigarette with a match, on top of ideo-motor apraxia , because of which the patient will never be able to complete the sequence and will remain with the match in his/her hands. The match will burn on and the PD patient, because of altered warmth/pain perception, will perceive pain late and will be exposed to the risk of burns. This evokes the need to teach the patient, through appropriate occupational therapy, to safely complete motor-sequences within ADLs and to interact with the environment in a risk-free manner (e.g. using pots and induction plates for cooking that feel cold). Central ataxia manifests itself as an altered processing of proprioceptive information which, after some authors, may be correlated to the onset of tremor and of their inability to precisely execute complex movements. Ataxia motivates the patient to use the sight for compensation purposes, especially as regards grasping and assessing the quality of an object. As the condition worsens, however, the sight reduces (diplopia, difficulty measuring distance), thus making this compensatory system useless. This is a time when the proprioceptive deficit and the ability to process the information coming from the hand are more obvious.

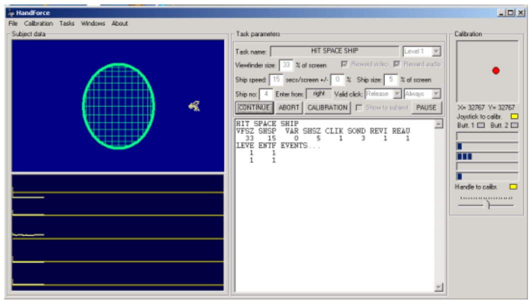
Our Study

They investigated the assumption that motor problems in the PD may be linked to cognition problems (36) (44) (69) with particular respect to set-shifting. If we consider this function from a motion- respect, the difficulty starting a movement may be seen as a difficulty shifting mental set: when faced with a situation, the patient is unable to shift from a motor-pattern to another and is blocked or tends to repeat the previous task by mistake. This prompted the creation of motor-cognitive tests, in order to emphasize an existing set-shifting deficit and impaired executional functions. It is also important to consider the influence of ataxia on the tests execution. In our study we selected and designed on pc these tasks, by taking into consideration the relationship between these deficits and the hand of the PD patient. In our assessment we are using a tool called "HandForce". It is a Joystick that can move in different directions, with pressure sensors on the fingers. With this tool, we can ask the patient to execute tasks while he/she is sitting in front of a screen and while combining motor and cognitive and proprioception-related functions. The tasks were chosen to be consistent with the use of the tool and sensitive to the neuro-motor deficits which are distinctive of PD patients and that typically affect normal hand functioning. The study shows how some difficulties, that these patients have controlling their hand are not primarily due to a motor deficit (e.g. akynesia), but may rather depend on ataxia and on a cognitive task-execution dysfunction. It is therefore clear that whatever the task proposed to the patient, particularly if it engages the hand cognitive- and neuromotor control system, it will be necessary to evaluate how and where the task is proposed, its content and the response to the task, while taking into account a complex combination of neuromotor, neurocognitive,and perception-elaboration issues. Before being exposed to the task, patients are rated through scales and screened base on their results: Hoen & Yahr (highest score: 1,5); Minimental State Examination (MMSE, rating not lower than 23). They will also be assessed based on the UPDRScale. Moreover we also tested hand apraxia by using some standard tests. We based our research-project on a pre-existing device, designed to complete tasks with a closed hand. We therefore felt the need to develop a new interface, that could support the same tasks with a closed or open hand . This represents the second step of the project that we are currently carrying out. In the business world, this can lead, for example, the difficulty in moving from one step to the next in the execution of a work task.

Tasks

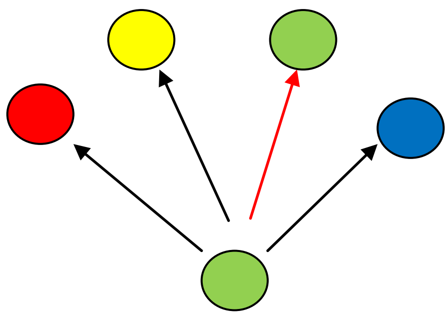
Here follows a concise list of the tests that we selected:

1."Shoot down the shuttle" : in this task the patient is asked to "shoot down the shuttle" by pressing a button on the joystick the moment it is on sight. The shuttle travels horizontally and at a constant speed. The purpose of the task is emphasizing the difficulty that the PD patient has reacting to a moving target, when the motion-pattern is predictable.

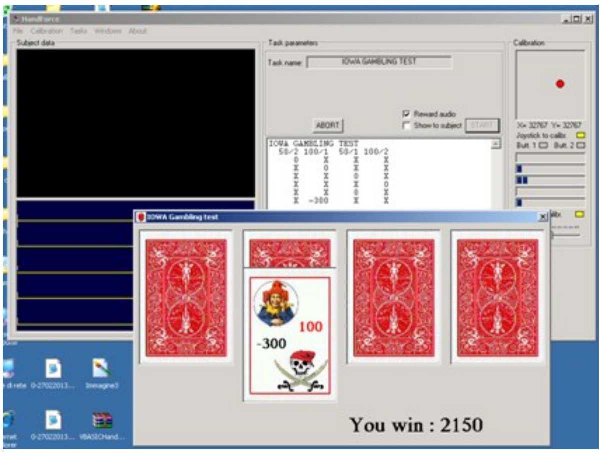


2.*"Star Wars"* : the patient is asked to aim the shuttle, which will show up at random along the Cartesias axes, and "to shoot it" without pre-establishing any trajectory, and by just moving the joystick, which is limited to the axes, into the appropriate direction. From a cognitive respect, this test requires the ability to execute self-shifting while repositioning the joystick and clicking to shoot and, from a motor respect, it implies the ability to correctly complete two gestures.

3. ***"Combine colours":*** this is the so-called Stroop Test. Yhe patient must move a coloured ball onto the word that means the corresponding color. From a cognitive respect, what we are trying to assess is the patient's ability to remain focused on a stimulus, while inhibiting interferences. From a motor- point of view we will ask the patient to autonomously follow a diagonal trajectory, as a way to assess precision, the impact of tremor and, more in general, the time needed to execute the task.



4. *"IOWA Gambling Test":* a card game that emphasizes how PD patients tend to impulsiveness and gambling. L'Iowa gambling task is a psychological test based on gambling (gambling English), used to observe the decision-making mechanisms of the human mind in real life. Designed by Antoine Bechara et al., It was used in several experiments aimed at analyzing the ability of choice deficient in patients with injuries ventromedial prefrontal and orbitofrontal cortex. Since it has been shown that lesions in these areas will be unable to recall the emotions related to past events,it is expected that patients are unable to benefit from previous experience. So, they will carry out their own choices in a completely random, without following a strategy game and chase the reward immediately, ignoring the negative stimuli caused by gambling losses. It will highlight then, an impulsive attitude and a tendency to gambling. (69) (70) (71)



5. *"Set Shifting Test"*: This test (36) (44) is composed of three parts: A) this part is mainly focused on motor-abilities; the patient is asked to learn and reproduce two different motor-sequences, by pressing the buttons of the Hand-Force ,ex. 1: index-middle-annular , ex 2) index-annular-middle finger. Cognitively the patient's difficulty to shift from one motor- sequence to the other is clear. From a motor-respect, the patient has troubles discerning and deciding single finger-movements. B) This is a more cognitive section: the patient is presented with a coloured geometrical shape (eithei red or green) and is asked to associate it, by pressing one of the two buttons, to its target of reference by colour or shape. This test specifically measures set-shifting abilities.

6. *"The Hanoi Tower"*: we propose a simplified version of this test (73) (only three discs).The discs are piled up around the first in three stick, to form a cone. The patient is instructed to reproduce the cone around the third stick, by shifting one disc at a time with the help of the joystick and is not allowed to put a larger disc on a smaller one. This is the "working memory test", whereby we measure the patient's ability to memorize previous moves and visualize his/her next ones , as well as the patient's shifting ability.

7. *"Trail Making Test"*: (72) it is administered in two ways. While moving the joystick the patient must: a) re-order a random list of numbers into a growing sequence; b) rank in a growing, alternate order a sequence of randomly distributed numbers and letters .This test serves the purpose of eliciting visual-spatial memory (in "a") and shifting abilities (in "b"). From a motor-respect, it helps assess shifting-speed and trajectory-precision.

8. *"Washing Dishes"*: (73)the patient is expected to design the right dish-washing sequence-trajectory. This test measures the ability to evoke the "working memory" and the patient's motor-ability to design the correct trajectory.

9. *"OK, the pressure is right!" :* The patient is exposed to three objects, (63) (73) one a time, made of different materials (cardboard, plastic, aluminium) . By using the pressure-sensors on the joystick, the patient is asked to apply the right pressure to the object , within a pre-set range, in order to grasp it without smashing it or letting it fall. This test may be also administered without the visual feedback from the pressure-bar or without showing the hand, according to the expected level of difficulty reserved for the patient. This test aims at revealing a possible deficit of proprioception or of the ability to modulate the hand-force.

Other possible applications This tool and other specific tasks could be developed to evaluate and to treat other neurological hand-related disorders. It also may be used to elicit specific cognitive impairments in elderly people. Assess cognitive ability in people with PD, engaged in potentially hazardous work.

Conclusions

The HandForce allows a rapid appreciation of the syndrome and dysexecutive and apraxia in people who do not experience a reduction in the use of the upper limb. These problems frequently occur in Parkinson workers who, despite not having a high motor symptoms, show a reduction in capacity cognitive manual and reducing the use of the hand in daily activities and work. In view of the need to keep the work commitment and given the prolonged retirement age, rehabilitation cognitive-motor allows these people to prevent the development of disability through a dialectic perceptual motor, making the movement of the hand to the task required in all activities of daily life.

Bibliography

1. Rajesh Pahwa, Kelly E. Lyons, "Handbook of Parkinson's disease" , 2007

2. Lees AJ. "Unresolved issues relating to the shaking palsy on the celebration of James Parkinson's 250th birthday". (2007).

3. Economo, C. (1917). "Encephalitis lethargica". Wiener Klinische Wochenschrift 30: 581–585.

4. Cruchet R, Moutier J, Calmettes A. (1917). "Quarante cas d'encéphalomyélite subaiguë". Bull Soc Med Hôp Paris 41: 614-6.

5. Stanley L. Robbins, "Le basi patologiche delle malattie"; traduzione italiana del dott. V. Eusebi e del prof. G. Frizzera, rivista e presentata dal prof. A. M. Mancini, Padova : Piccin, 1979, Vol. II, p. 1530

6. Reid AH, McCall S, Henry JM, Taubenberger JK (2001). "Experimenting on the past: the enigma of von Economo's encephalitis lethargica". J. Neuropathol. Exp. Neurol. 60 (7): 663–70.

7. Henry Ey, P. Bernard e Ch. Brisset, "I disturbi mentali dell'encefalite epidemica". In : Manuale di Psichiatria, III ed. ital., Milano : Masson Italia editori, 1983, pp. 892-898

8. Vilensky JA, Goetz CG, Gilman S (gennaio 2006). "Movement disorders associated with encephalitis lethargica: a video compilation". Mov. Disord

9. "Dopamina: dalla biologia alla clinica" (http:/ / www. stefanocanali. com/ CD_dopamina/ default. htm)

10. http://www.dukehealth.org/health_library/news/9904

11. Recettori dopaminergici (o della dopamina) | Farmacologia (http:/ / medicinapertutti. altervista. org/ argomento/recettori-dopaminergici-o-della-dopamina)

12. "Beyond the Reward Pathway". Retrieved (2009)

13. Pierce RC, Kumaresan V.. "The mesolimbic dopamine system: The final common pathway for the reinforcing effect of drugs of abuse?" Neuroscience and Biobehavioral Reviews 30:215-38 (2006)

14. Purves D et al.. "Neuroscience". Sinauer 4ed. 754-56 (2008)

15. www.parkinsonitalia.it

16. Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL (aprile 2008). "The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis". Mov. Disord. 23 (5): 631–40. DOI: 10.1002/mds.21922 (http:/ / dx. doi. org/ 10.1002/ mds. 21922).

17. Marsden CD, Fahn S: "Movement Disorders". London: Butterworths, 1981

18. G.U.Corsini, in Atti congresso Limpe (2009).

19. www.limpe.it

20. Mazzoni et al., "The persistent Mystery of the Basal Ganglia's Contribution to Motor Control" (2010)

21. Albin RL, Yong AB, Penney JB. "The functional anatomy of disorders of the basal ganglia". (1995) impulsivity". Am J Psychiatry 164: 4-6

22. Colosimo C.:" La Malattia di Parkinson e i disturbi del movimento". CIC. Edizione Internazionali, 2001.

23. PEZZOLI G., Tesi S.: "Guida alla Malattia di Parkinson". Associazione Italiana Parkinson, 2002.

24. de Lau LM, Breteler MM "Epidemiology of Parkinson's disease" . Lancet Neurol. 5 (6): 525–35. (2006).

25. A.Costa, C.Caltagirone "Malattia di Parkinson e parkinsonismi. La prospettiva delle neuroscienze cognitive" (2009).

26. Hoehn, MM., MD. Yahr . "Parkinsonism: onset, progression and mortality". Neurology 17 (5): 427-42. (1967).

27. C.H.Adler, MD,PhD "Nonmotor Complications in Parkinson's Disease" Parkinson's Disease an Movement Disorders Center, Department of Neurology, Mayo Ckinic Scottsdale, Arizona, USA (2005).

28. A.M.Bonnet et al., Review article: "Nonmotor symptoms in Parkinson's Disease in 2012: Relevant Clinical Aspects" Hindawi Publishing Corporation Parkinson's Disease Volume 2012

29. R.A.Armstrong "Visual Symptoms in Parkinson's Disease" . SAGE-Hindawi Access to Research, in Parkinson's Disease, Volume 2011

30. C.G.Goetz, MD, "Movement Disorder Society" (2008)

31. Kaufer, D.I., & Lewis, D.A. "Frontal lobe anatomy and cortical connectivity" (1999).

32. Stuss, D.T., Benson, D.F., 1986. "The Frontal Lobes". Raven Press, New York

33. Norman D and Shallice T (1986). "Attention to action: willed and automatic control of behavior". In: Davidson R, Schwartz G and Shapiro D, eds. Consciousness and self regulation: advances in research and theory,Vol. 4. pp. 1–18. New York, Plenum

34. Owen et al., "Spatial and non-spatial working memory at different stages of Parkinson's disease" . Neuropsychologia (1997).

35. Baddeley A. "Working memory" Oxford, Clarendon Press,1986

36. C.Caltagirone, A.Costa "La Sindrome Disesecutiva" (2004)

37. Lezak, M. D. "Neuropsychological Assessment." New York: Oxford University Press, 1995.

38. Barbulo AM, Grossi D. "Le demenze degenerative con preminente coinvolgimento frontale". In Grossi D. e Trojano L. Neuropsicologia dei lobi frontali. (2005)

39. Dubois B., Pillon B., "Cognitive deficits in Parkinson's disease" Journal of Neurology. (1997)

40. Thornton T. "Disexecutive syndrome: dealing with day- to-day decision-making" (2008).

41. M. Onofri, B.Perfetti et al., "I Disturbi Cognitivi" (2009)

42. Benton A.L., Costa L., Spreen O., "Studies in neuropsychology: selected papers of Arthur Benton", Oxford University. (1985)

43. Baddley A. "La memoria come funziona e come usarla" (1993)

44. Tinazzi M., Bombieri F. " Strategie cognitive e cueing nella Malattiad i Parkinson" Atti Congresso Limpe (2011)

45. Potenza MN "To do or not to do? The complexities of addition, motivation, self control and impulsivity". Am J. Psychiatry 164:4-6 (2007)

46. Hollander E, Cohen LJ "Impulsivity and Compulsivity" American Psychiatric Press Inc. (1996)

47. Di Chiara G. Atti congresso Limpe (2011)

48. Djamshidian A. et al., "Stroop test performance in impulsive and non impulsive patients with Parkinson's disease" Parkinsonism and related disorders. (2010)

49. Yi-Hsing Hsieh et al., "Cognitive and motor components of response speed in the stroop test in Parkinson's disease patients" (2008)

50. Di Chiara G. "Dopamina e Piacere" (2009)

51. Wise R.A. "Dopamine and Reward: The Anedonia Hypothesis 30 years on" . Neurotox Res. 14(2-3): 169-183. (2008)

52. Masayuki Matsumoto et al., "How do dopamine neurons represent positive and negative motivational events?" Nature (2009)

53. Abbruzzese G. "Apprendimento motorio nella Malattia di Parkinson" . Riabilitazione nei disturbi del movimento. (2010)

54. Zadikoff C. et al., Review article: "Apraxia in movement disorders". Brain (2005)

55. Leiguarda RC et al., "Apraxia in Parkinson's disease, progressive sopranuclear palsy, multiple system atrophy and neuroleptic-induced parkinsonism". Brain (1997)

56. Qureshi M. "Ideational Apraxia in Parkinson Disease" (2011)

57. King Lauren "A model based approach to apraxia in Parkinson's disease" (2010)

58. Kuan-yi Li et al., "The effect of dopamine replacement therapy on haptic sensitivity in Parkinson's disease". J Neurol 257:1992–1998. (2010)

59. Rabin E. et al., "Tactile/proprioceptive integration during arm localization is intact in individuals with Parkinson's disease". Neurosci Lett. (2010)

60. Mongeon D et al., "Impact Of Parkinson's Disease And Dopaminergic Medication On Proprioceptive Processing". Neuroscience158 . 426–440. (2009)

61. www.parkidee.it

62. Boisseau E. et al., "Eye-Hand Coordination in Aging and in Parkinson's Disease". Aging Neuropsycology and Cognition , vol.9, No.4 (2002)

63. Nolano M, Provitera V, Estraneo A, et al. "Sensory deficit in Parkinson's disease: evidence of a cutaneous denervation. Brain" ;131:1903–1911. (2008)

64. Jobst E. et al.,. "Sensory perception in Parkinson disease". Archives of Neurology; 54:450–454. (1997)

65. Zia S, Cody F, O'Boyle D. "Joint position sense is impaired by Parkinson's disease". Ann Neurol (2000) ;47:218 –22

66. Helmich R.C. et al., "Cerebral causes and consequences of parkinsonian resting tremor: a tale of two circuits?" . Brain (2012)

67. Vallet A. "Étude préliminaire d'un système pour la mesure semi-quantitative de la force de la main". Projet de diplôme Bachelor, Heig-vd. (2012)

68. Oury Monchi et al., "Neural Bases of Set-Shifting Deficits in Parkinson's Disease" The Journal of Neuroscience, 24(3):702–710 (2004)

69. Bechara A. et al., "Insensitivity to future consequences following damage to human prefrontal cortex". Cognition (1994)

70. Bechara A. et al., "The Iowa Gambling Task and the somatic marker hypothesis: some questions and answers". Cognitive Sciences. (2005)

71. Rossi M. "Decision Making in Parkinson's Disease patients with and without Pathological Gambling". European Journal of Neurology (2009)

72. Reitan R. M. "Validity of the Trail Making test as an indicator of organic brain damage". Percept. Mot Skills, 8, 271-276. (1958).