that most of the subjects delay more in recognizing a stimulus than it was not previously memorized.

Finally, they were obtained the assignment mistakes in each test by the studied subjects when were omitting to answer as well as when were making it defectively. The result of the study indicated that the AAD had more difficulty than the controls to recognize both types of stimuli: "target and "not target" increasing the differences between the groups while was making it the complexity of the test. At the same time, they were concentrated worse that the controls if take into account the greater number of answers omitted by the AAD with respect to the control group. In conclusion, and in spite of the time elapsed without using no drug, the AAD demonstrated to have more problems than the controls to accomplish the mentioned tests. This would indicate at least a decrease of the more basic cognitive functions of the AAD with respect to the control group.

181 THE PSYCHOPHYSIOLOGY OF OPIOID TOLERANCE AND DEPENDENCE

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Dependence can be conceptualized as the endproduct of series of behavioral and psychophysiological events that define how the simple animal organism react to an experimental environments where the substances of drug abuse are available. Tolerance and physiological dependence processes define the stages of the addiction cycles. The identification of multiple classes of opioid receptors -μ, κ, δ- and their subtypes (μ1-μ2) prompted investigators to use receptor-specific ligands to elicit the receptor mechanism of development of tolerance to and dependence on various receptor selective opioid ligands. As it is well known tolerance develops to virtually all opiate actions with chronic use although not necessarily at the same rates or to a same degree. To determine whether the differences in development of acute tolerance to several morphine actions correlate with the μ receptor type (subtype) mediating them, we have examined the appearance of acute tolerance to several opioid actions e.g. antinociception, respiratory depression and gastrointestinal transit in animals treated chronically with increasing sc. doses of 6-substituted morphine derivatives, elaborated by us, compared their actions to that of the corresponding parent compounds.

Certain compounds tested showed naloxonazine-sensitive μ-1 mediated analgesic action, in a dose range of 1.0–4.1 mg/kg, in the rat tail flick test. After chronic administration the tail flick latencies declined nearly to baseline levels, implying the rapid development of tolerance (dose ratios 3.8–6.4). In contrast the gastrointestinal action and their inhibitory influence on the respiratory depression induced by fentanyl, measured with arterial blood gas determinations, showed no significant tolerance after chronic treatment period. Also, the receptor mechanism of physical dependence appared to be μ_1 receptor dependent process. Thus, these results demonstrate that tolerance and physical dependence develop far more rapidly, than the naloxonazine insensitive actions and may help explain differences in the rate of tolerance and physical dependence development to opioid actions.

182 DISCUSSANT

P. Flor-Henry

SYMPOSIUM 31: Psychophysiological Perspective on Childhood Psychophysiology

183 PSYCHOPHYSIOLOGICAL PROBES OF ACUTE AND LONG TERM BRAIN NEUROTOXICITY DUE TO CHEMOTHERAPY AND RADIOTHERAPY IN CHILDREN TREATED FOR LEUKEMIA

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In children treated for acute lymphoblastique leukemia (ALL), cranial radiation therapy (CRT) and intrathecal chemotherapy (ITC) decrease the risk of meningeal relapse. However, this prophylactic treatment leads to cognitive sequelae. Auditory ERPs were used in a passive condition in order to monitor brain functional neurotoxicity during and after treatment. The response was larger for the rare stimuli and displayed a large negative fronto-central wave peaking between 220 and 250 ms, and a temporal wave peaking at 160 ms. In a cross-sectional study, on average 2,5 years after treatment completion, 7-to-11 year old girls treated with ITC, with combined CRT and ICT showed reduced amplitude of the two components, especially on the frontal sites, as compared with normal controls. In a longitudinal study, N1 amplitude decrease related to CRT/ITC suggest that ERP could be useful to assess acute brain irradiation harmful effects, and to predict and evaluate the functional late sequelae.

184 IS A DEFICIT IN TIMING CONTROL A CENTRAL DYSFUNCTION UNDERLYING DEVELOPMENTAL DYSLEXIA?

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